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Roentgen Therapy in the Management of Some Non-Malignant Diseases Affecting the Organs of the Female Pelvis[1]

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ENDOMETRIAL hyperplasia, endometriomata, and myofibromata constitute what appears to be a rather closely related group of tissue changes whose origins depend upon a common factor (estrin). Because of the increase in their incidence in recent years, these conditions warrant intensive investigation and consideration from the standpoint of diagnosis and treatment. That the frequency with which they are encountered in gynecological practice is increasing, there can be little doubt. The explanation of this increase is not so clear, but it is claimed that delayed marriages (2) and lack of early and frequent childbearing are factors of great importance, if not the primary cause.

The term management, as used in this paper, implies the adoption of a procedure for case handling based upon an understanding of the etiology and the nature of the disease changes as well as the selection of the most desirable method of treatment and its application. Before discussing therapy for these conditions it is logical and appropriate to consider their pathology and diagnosis.

PATHOGENESIS

Endometrial Hyperplasia: Cystic glandular hyperplasia, or endometrial hyperplasia, is characterized by disturbances of the menstrual flow and the presence of glandular cystic hyperplasia of the endometrium. These changes appear to be the result of the action of the ovarian follicular hormone—estrone—and the absence of progesterol. The work of outstanding investigators (4) seems to prove conclusively that long-continued estrin stimulation of the endometrium, produced by ovaries with multiple follicular cysts and without a corpus luteum, is the cause of the characteristic cystic glandular hyperplasia of the endometrium, resulting in what is commonly known as the "Swiss cheese pattern." There is little doubt that the influence of the gonadotropic hormones of the pituitary body is also in some way a factor in this physiological disturbance.

Endometriosis: Endometriomata and endometriosis are conditions in which endometrioid tissues are found in ectopic locations. There are two main types of endometriosis. One is characterized by a down-growth of the epithelium into the myometrium, or the occurrence of islands of endometrial epithelium and stroma interspersed among bundles of smooth muscle tissue, entirely separated from the true endometrium. The latter are usually found in women who have been pregnant. This extension may involve almost the entire uterus, and if fibroids are present

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even these may be invaded. This condition has been designated adenomyosis.

In the other type of endometriosis, endometrioid tissue is found in the ovaries, the oviducts, or somewhere on the pelvic or visceral peritoneum, most frequently in the cul-de-sac, on the anterior surface of the uterus, the uterosacral ligaments, etc.

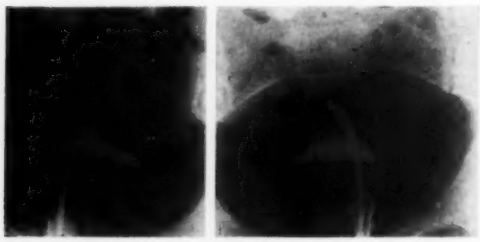

Fig. 1. Endometrial hyperplasia, indicated by finely serrated margins, most marked on the superior margin.

When symptoms first appear, the lesion is likely to be localized, but after operative manipulation it may extend and invade pelvic viscera, cover the entire pelvic floor, and present a firm pelvic mass to palpation, simulating a malignant neoplasm.

Many interesting theories have been offered to explain the presence of endometrioid tissues in these unusual locations. One of the most plausible is that of menstrual spill into the pelvis (3), or the retrograde flow of the products of menstruation through the oviduct into the pelvic cavity and subsequent transplantation on the peritoneal surfaces of the viscera or into the ovary at a point where a follicle has ruptured. Some investigators are more inclined to support the embryological theory (2). Since the mucosa of the cervix, oviducts, endometrium, and pelvic peritoneum have a common origin in the celomic epithelium from the müllerian tract of the embryo, it is possible that any of these tissues may still contain groups of embryonic cells which, under certain conditions of stimulation, may multiply and produce a more or less normal adult tissue in an ectopic location. It is obvious that ectopic tissues of the endometrioid type would manifest the same physiologic response to the stimulating influence of estrin and progestin that characterize true endometrial tissue in its normal location. Repeated intervals of menstruation over a long period, without the interruption of the cycles by pregnancy, are probably not physiological. The monkey exhibits a menstrual cycle almost the same as in woman, but in the natural state it is not likely that menstruation occurs very often after maturity and mating begin. It seems reasonable to assume that endometriomata are not true tumors, but that they represent tissue changes arising from a disturbance of physiology which is concerned with late marriage and delayed or infrequent childbearing, which should occur to interrupt long periods of continuous cyclic menstruation.

Myofibromata: So-called myofibromata are really leiomyomata, that is, composed of smooth muscle and fibrous tissue. It is generally accepted that the primary growth is myomatous and the connective-tissue proliferation is secondary. When a diagnosis of myofibroma is revealed, the first question from the patient is almost invariably, "What is the cause?" At present we are obliged to answer with some vague generality, for as yet the true etiology remains unexplained.

No one doubts the intimate relationship between menstruation and the development of myofibromata. They occur after puberty and are located in that part of the uterus which is concerned most actively with the menstrual function. There is an abundance of evidence in clinical practice and in the field of research which would couple the development of myofibromata closely with endometrial hyperplasia and endometriomata (4), and would strongly suggest that all are the result of a physiological disturbance, with hyperestrinism as the most important factor. Multiple subperitoneal myofibromatous growths and also adenomatous hyperplasia of the endometrium have been produced in guinea-pigs (7) by injecting large amounts of the ovarian hormone. When we consider that

careful histogenic studies of fibroids have failed to reveal the presence of any characteristic myomatous embryonic cell that could in some way be traced to the developing myoma, together with the fact that histological research has shown that the earliest microscopic evidence of myoma is hyperplasia within a bundle of smooth muscle cells, which appear in every way to

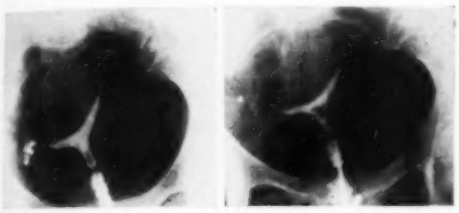

Fig. 2. Polyp located near the internal os, indicated by the displacement of contrast material at this point.

be normal, we must admit that the weight of evidence strongly favors estrogenic action as the cause of uterine myofibroma.

Further evidence is to be found in the histologic similarity between diffuse hypertrophy and gestational hyperplasia, on the one hand, and early myofibromata on the other hand. The growth-stimulating agent, whatever it is, disappears when the ovaries are removed, and the uterus proceeds to regress into its post-climacteric state but, as has been shown by a large number of investigators, the endometrial cavity and the corpus uteri enlarge when the estrogenic hormone is administered after castration.

DIAGNOSTIC CONSIDERATIONS

The cardinal symptoms of myofibromata are hemorrhage, sterility, and pressure distress in the pelvic region. Hemorrhage is usually first considered as a prolongation of the periodic menstrual flow. The blood loss, at times, may be enormous. Bleeding between the menstrual periods and increased menstrual flow always warrant immediate and adequate investigation.

The detection of early changes in the endometrium becomes possible in many cases at a time when symptoms are relatively mild in character, and the functional and anatomical damage is slight. Diagnostic investigation should almost invariably include studies with the fluorescent screen and with films (8, 9) made following introduction of contrast material into the cavity of the uterus. The character of a defect in the endometrium, as disclosed in an x-ray examination, offers important data for the differentiation of the lesions causing uterine hemorrhage. After the menopause, hemorrhage most frequently denotes the presence of a malignant condi-

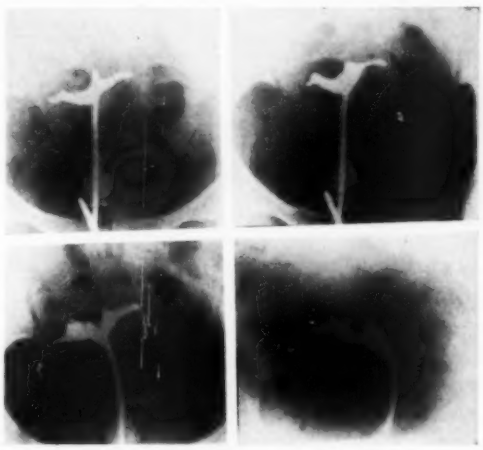

Fig. 3. Small submucous myofibromata, indicated by smooth distortions of contour of the endometrial cavity shown here with different positions and quantities of contrast material in the same patient.

tion, but just as in premenopausal hemorrhage, roentgen studies are exceedingly useful in conjunction with biopsy and other investigations upon which we must depend for the final diagnosis and for the formulation of a rational plan of management.

Observing a uterogram, we may find a finely serrated outline and globular appearance at the margins or on the surfaces of the endometrium, a defect caused by endometrial hyperplasia or polyp formations (Figs. 1 and 2). These findings appear in marked contrast to the smooth impinging defects of the smaller submucous or intramural myofibroma. In this condition, the usual triangular form of the cavity is more

or less disturbed and the margins and surfaces may also be irregular (Fig. 3). Finally, the elongated cornu and completely distorted but smooth outline of the cavity of the corpus uteri seen in the presence of large fibromata (Fig. 4) are easily differentiated from the very irregular notched and highly grotesque outline observed when a malignant process has advanced sufficiently to produce symptoms (Fig. 5).

Fig. 4. Myofibromata of great dimensions causing extreme distortions of outline and position of the endometrial cavity and cervical canal.

As in the investigation of other disease entities, it is most important first to consider carefully the patient's history and the findings elicited in a complete physical examination. With these data available, such special examinations as may be required can be recommended and conducted, and the proper type of treatment can be advised.

TREATMENT

The age of the patient may influence our decision as to the plan of treatment in these cases. In the case of the younger woman, that is, in the twenties, we are fortunate to have the science of endocrinology making such rapid strides in the control of symptoms, for it is always undesirable to institute radical measures at this period. The picture changes in the thirties, especially in the late thirties, when radiation castration and radical surgical operation upon the pelvic genital organs become rational procedures.

The patient's attitude toward pregnancy and childbearing may influence the plan of treatment in the management of these cases. The desire to bear children, even in the presence of myofibromata and other pathological conditions that might interfere with the process of labor after conception has been achieved, is one of our greatest problems. If we agree that the conditions under discussion are primarily disturbances of normal physiological processes, and that contraceptive measures adopted immediately following marriage have accounted, in recent years, for increasing numbers of women with long periods of uninterrupted menstrual cycles and the sequel of continued hyperestrinism, it then becomes our duty to consider instituting any measure to promote conception and childbearing at this period. In

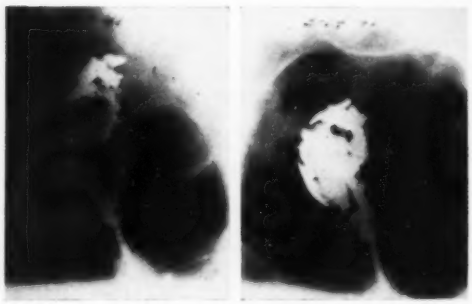

Fig. 5. Corpus carcinoma showing complete loss of normal outline, in marked contrast to defects due to benign conditions.

adopting this point of view, a physician can fully justify his position in urging women after maturity (twenty-three years) to marry and to bear children as early as possible and, if contraception is to be practised, to withhold it until at least the fourth decade of life has been reached.

In the final arrangements for therapeutic management of these cases, remedies which have long been in general use must not be overlooked, as the judicious use of ergot, stypticin, extract of the pituitary and suprarenal glands, calcium, rest in bed, the application of ice bags, intrauterine and vaginal packing with gauze, rubber, and other substances, blood transfusions, etc.

Certain surgical procedures which do not create an artificial menopause are

justified and should be instituted, even when the correction anticipated is trivial, temporary, or inadequate. I refer to careful cervical dilatation with perforated sounds and the excision of polyps and other diseased tissues along the cervical canal and in the endometrium which may be causing mechanical irritation, atresia, stenosis, or periodic blocking. Electrosurgical methods (10) should be employed in this work almost exclusively. In a small proportion of cases, laparotomy is justified, with a view to removing certain pedunculated fibroids and those so located that they impinge upon the normal birth canal with the possibility of subsequent dystocia. In these cases the surgeon can feel free to leave the ovaries intact, for when the results obtained do not accomplish all that is desired, final relief can always be secured through irradiation after all hope of childbearing has been lost.

It is understood that the full correction of the conditions under discussion is accomplished only when the menopause is complete. From the physiologic standpoint, it would seem that there is little or no difference whether the menopause is natural, artificial, induced by radiation, or the result of surgical ablation of the pelvic genital organs. While the physiologists seem to agree that the gonadotropic hormone of the pituitary body appears in the urine in the same manner after castration by either of the artificial methods or the natural menopause, and while they also believe that the sexual characteristics of the patient will, or should, remain the same after castration by radiation or surgery, there are clinical investigators who hold that normal sexual qualities are better preserved through the years of life that follow the climacterium, when the permanent interruption of menstruation has been acquired through irradiation rather than by the removal of the pelvic organs.

In the presence of endometriomata, operative intervention must include removal of all ovarian tissue, or the surgeon faces the possibility of creating a progressive endometriosis as a postoperative misfortune. Chocolate cysts of the ovaries are frequently bilateral and, even when no other evidence of pathology is present in the pelvis during abdominal section, the partial excision of the visible cystic portions of the ovaries carries the hazard of a progressive endometriosis.

Among the conditions that have been considered as contraindications to irradiation castration are pelvic infection and serious complicating pelvic pathology (ovarian cysts and tumors), especially large, calcified, or pedunculated fibroids, etc.

In the plan for treatment, whether it be surgical or radiological, it must first be decided if cessation of menstruation is required, and if it is to be temporary or permanent; second, if surgery or irradiation shall be employed; and third, if irradiation is decided upon, whether it shall be with x-rays, radium, or both.

Where temporary menolipsis is desired, radium may be chosen because of its more intense action on the uterine mucosa and diminished action upon the ovary. Where permanent castration is necessary, x-rays may be preferred because of their greater action upon the ovary and other tissues of the pelvis, especially in cases of endometriomata. For this reason radiation castration may be selected rather than surgical ablation of the ovaries. Furthermore, an undesirable response in these ectopic tissues to the stimulating effect of estrogenic remedies given to allay severe postclimacteric symptoms may be expected after a surgical castration. The dosage and the method of application should be determined by the experience and radiological practice of the physician who is to administer the treatment.

Radiotherapists quite generally agree that about 300 r delivered into the pelvis are required to produce menolipsis at the beginning of the fourth decade of life. When radium is employed, about 500 mg.-hr. must be delivered to the endometrium, with the usual filter and plain applicator. Where pronounced action upon the endometrium and myometrium, as well as any ectopic endometrioid tissue

located in the pelvis, is desired, at least 1,000 r should be given into the pelvis, followed by radium, 1,000 mg.-hr., within the endometrial cavity and the cervical canal. A detailed discussion of the modifications of technic for irradiation in different groups of cases would require more space than is available here.

In our clinical work we note that there has been a gradual transition from surgery to irradiation in the management of this group of non-malignant conditions of the pelvis, and it would appear that, as more reliable methods of diagnosis are becoming available, a still greater percentage of our cases will be subjected to irradiation rather than to surgery.

SUMMARY

1. Certain non-malignant conditions in the pelvis appear to have a common factor in their etiology.

2. Regular recurrence of menstruation over long intervals, without interruptions by pregnancy, is probably not physiological, and, with the consequent hyperestrinism, may be responsible for the pathological conditions discussed in this paper.

3. The growth-stimulating action of estrin is lost by castration.

4. Parents are justified in urging early marriages and childbearing with the hope of checking the rising rate of frequency of these diseases.

5. Where the hope of childbearing has been lost through the presence of these diseases, production of an artificial menopause is justified.

6. Roentgen examinations of the uterus are almost indispensable for early diagnosis of these conditions.

7. Radiation not only checks follicle formation in the ovary, but also exercises a useful therapeutic action on any pelvic tissue that may be responding to endocrine stimulation.

8. Endometriomata may remain active following unilateral adnexectomy.

9. After oophorectomy quiescent endometriomata often react to hormone administration.

10. With adequate irradiation of aberrant endometrial implants distressing postmenopausal symptoms may be controlled safely by administering sex hormone products, stilbestrol, estradiol, etc.

11. Mortality from castration by irradiation is exceedingly low.

12. It is possible to produce a temporary menolipsis by irradiation.

13. Surgical removal of fibroids to relieve obstruction of the birth canal is always justified.

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DISCUSSION

Alson Kilgore, M.D. (San Francisco): It is an honor to discuss this paper, not as a radiologist nor as a gynecologist, but simply as a physician facing the problems of diagnosis which these conditions bring to the doctor's office every day. Small submucous fibroids, which cannot be felt on physical examination, polyps in the endometrium, which we sometimes miss even on curettage, and the common condition of endometrial hyperplasia are not easy of differentiation. If we can find a means of more accurate diagnosis of these conditions, it will be a material help.

I should like to ask Doctor Orndoff if he has observed any unfavorable effects from the injection of contrast material and whether leakage into the pelvis constitutes a danger.

As to the suggestion, which I have heard from at least one other well known gynecologist, that we attempt to change the habits of the American people in the matter of early marriage and more frequent childbearing, I strongly suspect that, as in the case of most idealistic campaigns of advice to the public, what we may say will have little influence, and that these matters will continue to be regulated by the conflict between the well known biological urge and the economic conditions in which we find ourselves.

Ira I. Kaplan, M.D. (New York): I know little about the diagnostic principles that are accepted by the radiologist in defining conditions within the uterus. I feel, as does Doctor Orndoff, that suppression of normal or abnormal uterine function by irradiation is not anything that we have nowadays to fear. I firmly believe that there is a biological and physiological difference between the patient who has had the ovaries surgically removed and one in whom ovarian action has been suppressed by irradiation. Whether the radiological effects are due solely to endocrine control or to the direct action of the rays on the endometrium or on the ovary, has not yet been worked out conclusively. We do know that all three of these factors have been observed in all types of cases. In a large general municipal hospital, where we have to take care of a great many young women, married and unmarried, with functional disturbances of the uterus, surgical castration is not always economically possible nor is it desirable. We must have some means of sterilizing these women so that they can carry on their daily life without the interruption necessitated by operative procedures and hospitalization. Irradiation offers such a method.

Just how long we can control normal physiological changes is uncertain. My associates a few years ago published a study of the time element in the control of ovarian and uterine function. They showed that the younger the patient the less drastic and the less permanent the sterilization and that, even though physiological activity was later resumed, the pathological condition was not reactivated. That is the important factor, and one worth remembering.

Whether early marriage means the relief of these conditions I do not know, for often we see sterile women with functional disturbances which are relieved by irradiation, who subsequently become pregnant.

Endometriosis is a large subject and hardly one that I can enter into now. Doctor Orndoff properly suggests that, in spite of removal of an involved ovary, endometriosis may still exist elsewhere in the body and the functional distress may continue. In such cases radiation therapy is certainly the method of choice.

Robert R. Newell, M.D. (San Francisco): I would like to have Doctor Orndoff correct me if I am wrong in my belief that endometriosis, in spite of the increasing incidence which he mentions, is still an uncommon disease.

As to the encouragement of early marriage and frequent pregnancies, I suggest, purely academically, that the young women of childbearing age are in less danger from endometriosis in this country than the young men of military age are in danger from the population pressures incident to early marriages and frequent childbearing in the over-populated countries around us.

Although endometriosis is an uncommon condition, cancer is a common one, and I would like always to be well assured that the particular patient we are dealing with is not suffering from cancer.

Doctor Orndoff mentioned the possibility of a temporary interruption of the function of the ovaries. In the interests of coming generations, I believe it is extremely unwise for any radiologist to injure the ovaries of a woman in whom ovarian function may afterward be restored and pregnancy occur.

Milton Friedman, M.D. (New York): In the treatment of carcinoma of the corpus uteri, one of the major difficulties is our lack of knowledge of the exact distribution of radiation around radium foci in the uterus. We therapists would certainly appreciate it if other roentgenologists would adopt Doctor Orndoff's precise radiographic technic, which provides more exact information of the extent of the lesion to be treated with radium.

In response to Doctor Newell's last statement, I question how seriously the ovary is injured by temporary castration or by small doses of x-rays given with the intent to stimulate. I have had several comprehensive conversations with Doctor Henshaw of the National Cancer Institute, who has recently reviewed not only the experiences of others but his own extensive investigations. We intentionally approached the subject of possible damage to the ovary from totally divergent points of view: he from the standpoint of biological experimentation, I from the point of view of the clinical radiotherapist who does not see the injuries which the biologist says he should see. After our differences were whittled down, there remained four reasons suggesting that small amounts of radiation probably would *not* injure future generations:

First, there is a tremendous species difference. There is a wide variation in the amount of radiation necessary to produce genetic damage in Drosophila, mouse, rat, and guinea-pig, which have been the objects of most of the experiments. Were we to calculate exponentially from these experiments the dose necessary to produce mutations in man, the inevitable conclusion would be that it is impossible to damage the human ovary with the doses ordinarily used.

The second and very important fact is that radia-

tion mutations are by definition essentially irreversible, and once a radiation mutation is produced, it is persistent throughout future generations. Most of these radiation mutations, however, are lethal and disappear.

Third, Snell, in a study of the dangers of radiation, published a little over a year ago, failed to stress in his conclusion one very important fact: having exposed embryos to radiation and produced mutations, he varied that experiment and found that, if he irradiated the ovary, a certain number of mutations would occur after a given length of time, but after progressively longer times, fewer and fewer mutations appeared. In other words, there was a recovery element. Apparently some sublethally injured mutation forms, if given enough time, will die. The ovary as a whole recovers and produces normal germ cells. The clinical implication is that if an ovary is exposed to radiation for any reason, the patient should be instructed to refrain from conceiving for a certain length of time. Theoretically, and probably actually, her chances of ever giving birth to a monstrosity would thereby be considerably reduced.

Finally, Muller, upon whose work the science of radiation genetics is founded, recently stated, on the basis of his own investigations and statistical surveys, that, so far as the human race is concerned, the probability of producing radiation mutations as a result of small or moderate doses of radiation to the ovary is so slight that it can be considered negligible.

Doctor Orndoff (*closing*): There is really little for me to say, since so many questions have been fully answered by other discussants. One point has been raised, however, in reference to the possible effect of the contrast material which may enter the pelvis when there is a backspill from the endometrial cavity through the oviducts. I believe I can state that in not a single case has any serious development occurred; in fact, we have come to disregard this point almost altogether. For many years in the earlier part of our work, I endeavored to watch carefully for undesirable late developments. At that time cases upon which this work was done were selected very carefully. Later practically all classes of cases were taken in which the history and other findings seemed to need the support of uterography. In general it seems fair to say that we have encountered little or no untoward effect of any sort. Even in cases studied after conception the contrast material which passed through the oviducts into the true pelvis remained throughout the period of gestation. After parturition it disappeared from the pelvis promptly, while the reduction during the period of pregnancy could scarcely be detected. It would appear that acute inflammatory reactions constitute a real contraindication, but in such cases this type of examination is seldom required.

Radiation in Cancer of the Corpus Uteri[1]

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CARCINOMA OF the cervix is today definitely a radiation problem, but few cases being treated by radical surgery as originally developed by Werthheim. Irradiation has shown excellent results, consistently better than those obtained surgically, so that it is today the method of choice. Quite different is the situation with regard to treatment of cancer of the body of the uterus.

Except in advanced cases, surgical treatment has long been considered the method of preference for cancer of the uterine corpus. The ready accessibility of the uterus to surgical approach, its thick muscular structure, the slow extension of the disease to the surrounding parts, and the infrequency of early metastatic involvement have all served to make surgery the first choice in the treatment of this condition. Meigs (1) says: "The treatment of carcinoma of the body of the uterus is quite definite, total hysterectomy," and this is a dictum that has been followed in most clinics up to the present time. Carcinoma of the uterus appears most commonly after the menopause, when patients are still well able to stand radical operation.

One of the factors militating against irradiation in these cases was the inability of the early radiologist to secure a cancericidal dose sufficient to destroy the whole lesion. The faulty technic formerly employed in applying radium within the uterus often left many areas unaffected while other parts were actively destroyed. Recurrence was frequent, although both patient and doctor had been lured by the absence of symptoms into the erroneous impression that a cure had been effected. It is true, as Meigs states, that radium therapy in the body of the uterus is something of a blind affair, and that it falls short of the ideal treatment for uterine cancer, for, as Fricke (2) has said, one is trying to destroy a hidden cancer in an enclosed cavity. Even so, good results have been achieved by irradiation.

Another objection advanced against the use of radiation therapy is found in the prevalent belief that only certain types of malignant tissue respond to radiation. It was thought that cancers of histologic grades I and II were particularly radioresistant and that hysterectomy was therefore the only proper treatment. In 1930 Healy and Cutler, quoted by Healy (3), showed that not all adenocarcinomas of the uterus are of the same cellular structure, and that varying degrees of malignancy and radiosensitivity are encountered. In Healy's opinion a histologic diagnosis of grade I or II at the time of curettage justified immediate hysterectomy without preliminary roentgen or radium irradiation. But Healy and Brown (4) state that "under radiation therapy the degree of malignancy as determined histologically does not appear to be as important a factor in prognosis as it is when surgery alone is the method of treatment." Fricke and Bowing (5), on the other hand, consider the stage and histologic structure of the tumor of prognostic significance and state that the radium cure rate varies with the extent of the lesion and the microscopic grade.

Clinical radiation therapists have lately been able to disprove the assertion that uterine carcinomas of grades I and II are radioresistant and have actually demonstrated their favorable response to properly administered radiation. Fricke and Heil-

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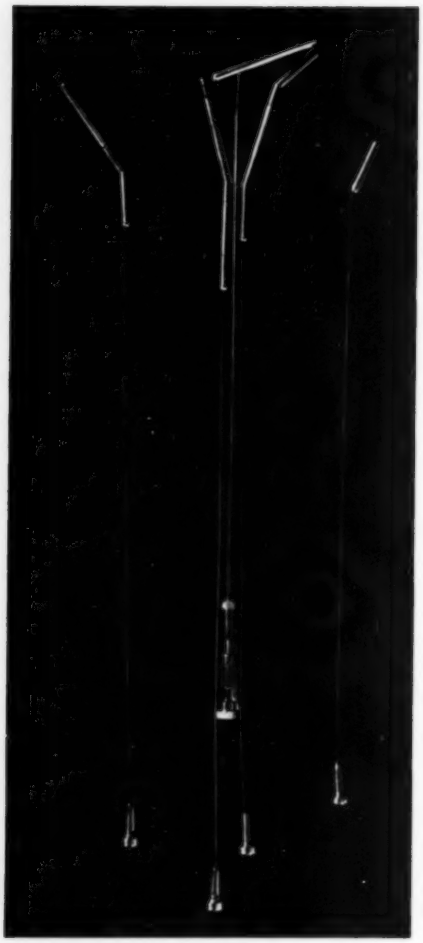

Fig. 1. Friedman "hysterostat."

man (2) report 39 per cent five-year cures in this group, while Fricke and Bowing (5) state that, in spite of the general opinion, tumors of lower grade are responsive to radium therapy and give the best chance of cure with this procedure. In many instances, however, irradiation alone is reserved for the poor operative risks and advanced cases. These obviously do not furnish a proper basis by which to judge the comparative merits of irradiation and surgery. Miller (6) has shown definite results substantiating this fact.

Heyman and his co-workers (7) report the results of their improved method of irradiation for the treatment of operable uterine cancer, showing an improvement of 20 to 30 per cent over results obtained with their previous methods. Of the clinically operable patients treated by them with irradiation, 75 per cent were alive and free of disease five years after the beginning of treatment. They also found, contrary to the opinion erroneously set forth by others, that hysterectomy may still be employed successfully should irradiation fail to control the disease in an otherwise operable case. Healy and Brown (4) report a five-year survival of 39 per cent in a series of 96 patients treated by irradiation alone; of their operable patients thus treated, 56.3 per cent lived more than five years. In a smaller group—8 patients—treated by irradiation and hysterectomy, Healy obtained a 100 per cent five-year survival. Scheffey (8) states that 50 per cent of his cases were successfully treated in this way.

The question of whether or not to rely on irradiation alone for the treatment of carcinoma of the uterus has not yet been entirely settled. Burnam (9) in 1931 stated that irradiation even in operable cases gave as good results as the best surgical treatment. Heyman (7), in 1941, was of similar opinion. Miller (6) advises irradiation followed by total hysterectomy as the procedure of choice for operable cases and with this method he has succeeded in obtaining a 70 per cent five-year survival rate. Brindley (10) reports a survival rate of 41.9 per cent with irradiation alone and 79.1 per cent with irradiation and surgery. Healy (4), on the other hand, believes that a 90 per cent cure can be secured by surgery alone in operable cases of histologic grades I and II, but that in other cases preoperative irradiation is of definite value. He also states that "radiation therapy offers a valuable form of treatment, adequate for cure in many cases where hysterectomy cannot be utilized." Miller (6) and Fricke (2) have shown that cancers, even of grades I and II, are responsive to irradiation. Scheffey (8) of Jefferson Medical College Hospital reports advantageous results following ir-

radiation with subsequent panhysterectomy.

It is generally agreed that in order to control the disease in cases of a high grade of malignancy preoperative irradiation is essential. In a group of 8 cases in which hysterectomy was done following intrauterine radium therapy, Friedman (11) found no residual cancer in 7. Brindley (10) properly states that the extent of the disease is the most important factor modifying the result, since most early lesions are curable regardless of the degree of cell activity. In his opinion hysterectomy following irradiation is a procedure carrying a very low mortality and a high percentage of cures in carefully selected cases.

During the past few years it has been our practice at Bellevue Hospital to irradiate operable uterine cancers, following this treatment with hysterectomy six to eight weeks later. Inoperable cases are treated by irradiation alone.

The problem of proper and effective treatment of cancer within the uterus is technically different from that of cancer of the cervix. The latter, because of its accessibility, permits more intensive direct application of radium to the local lesion. In cancer of the body of the uterus, the malignant involvement is in most instances situated within a small cavity entirely surrounded by a thick muscular protective wall, quite radioresistant, itself within the pelvis through whose wall external radiation must travel and be absorbed to a great extent before reaching the destined site. In Germany, where radium has not been readily available, primary reliance for irradiation has been placed on x-rays. Wintz, the leader in this work, has reported startlingly effective results in the treatment of uterine carcinoma with x-rays alone. His results and those of his followers have apparently not been duplicated by therapists in other countries employing his technic. As a preoperative measure, x-ray therapy has proved of definite value, but as Healy (12) has stated, it should not be considered curative.

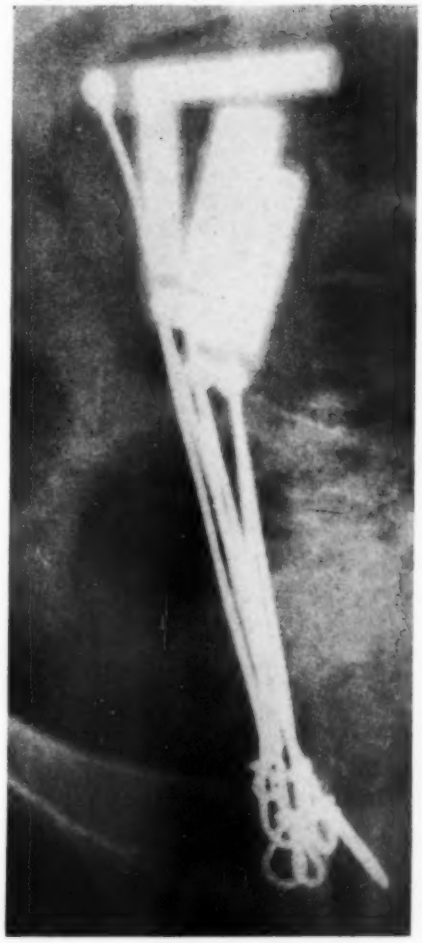

Fig. 2. Martin radium applicators.

From the radiation standpoint, the most efficient attack on uterine cancer is by direct intrauterine radium therapy. Martin (13) recommends intensive radium therapy as the primary procedure in all cases of uterine carcinoma. The problem is one of technic—how best to irradiate homogeneously and completely the whole endometrial area of the uterus. The original procedure of inserting a single sound containing various amounts of radium left much to be desired, for it seldom affected more than the directly adjacent tissues.

Many methods have been suggested for

utilizing multiple foci within the uterine cavity. Each of these, according to its advocate, was designed to provide a better application of the radium to the whole lesion. Friedman's ingenious method (11)

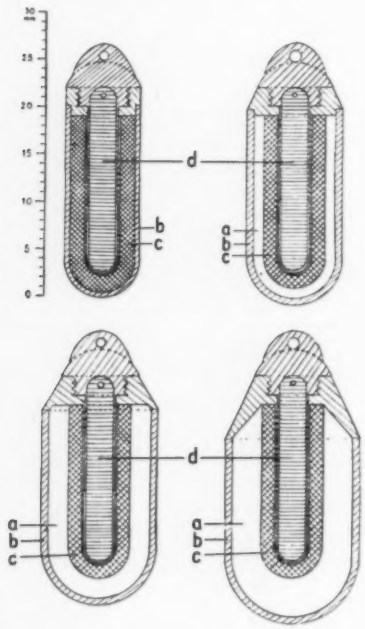

Fig. 3. Diagrams of irradiators of four different sizes designed for intrauterine radium application. *a*. Intermediate space filled by air. *b*. External wall of stainless steel. *c*. Inner wall of lead. *d*. Radium tube. (From Heyman.)

of multiple mechanical foci seemed to fulfill the requirements of effective radium application most satisfactorily. His applicator, the "hysterostat" (Fig. 1), represents an attempt to meet the geometric requirements of uterine cavities of irregular sizes and varying shapes. It consists of a crosspiece and several lateral tandem inserts, to the ends of which are attached stainless steel shells to hold the radium. It has the disadvantage of being somewhat complicated and not readily utilized by the inexperienced worker. Martin (13) and Pfahler (14), who recommend irradiation as the primary procedure in uterine cancer, for the large uterus use multiple radium applicators, Martin's consisting of small radium capsules (Fig. 2) attached to long tubes by hinges, and Pfahler's of capsules attached to wires and applied directly to the uterine cavity. Fricke (2) uses brass tandems in the depth of the uterus and in successive treatments in the mid and anterior portions of the canal. Heyman (7) of Stockholm has devised a much more elaborate method of multiple foci applicators (Fig. 3) for intrauterine treatment.

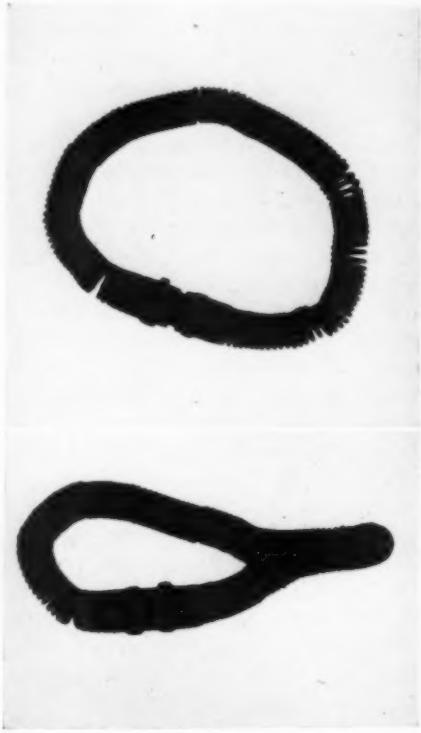

Fig. 4. Radium ring, open and folded for insertion into the uterus.

In this method the uterus is packed with several "irradiators" of uniform size, shape, and of equal radium content. Auxiliary filters of varying thickness are provided to fill up the space in the uterine cavity and an ingenious tube holder is used to insert and hold the irradiators in place. Heyman reports excellent results with his method.

Because of the present complicated tech-

nic and elaborate applicators, we have endeavored to find some simpler means of radium application which would meet the requirements of ready accessibility and easy application—an applicator which would lend itself to uterine cavities of all shapes and sizes and readily and effectively apply the radium to the whole cavity, covering all possible malignant foci.

At the suggestion of Dr. I. C. Rubin, who has demonstrated by x-ray studies the accommodation of the von Grafenberg type of silver ring within the uterine cavity, a similar device has been developed for holding radium tubes (Fig. 4),[3] which permits not only of easy insertion into the uterine cavity but also direct-contact irradiation of the malignant areas. This applicator will be described in detail in a later presentation.

Following the work of Rubin (15) on the radiographic study of the uterine cavity, we endeavored to determine its contour before planning the type of radium applicator to be used. With viscorayopak,[4] a readily absorbable contrast medium, it was possible to outline the uterine cavity roentgenologically and to recognize the presence of carcinoma, submucous fibroids, polyps, or other deformities. An example of the irregular formation suggestive of tumor growth is shown in Fig. 5. In Fig. 6, the radium ring is seen molded about the tumor. By means of such contrast pictures it is hoped to be able to gauge more accurately the type and amount of radium to use in therapeutic procedures.

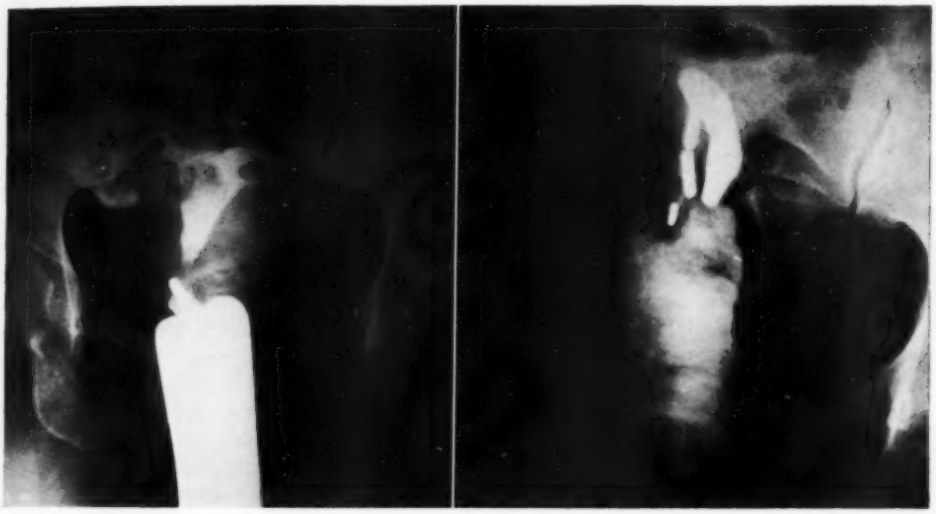

Fig. 5. Hysterogram made before radium insertion, showing irregularity within the body of the uterus.
Fig. 6. Same case as shown in Fig. 5, with radium ring molded about the tumor in the uterus.

For inserting the radium ring the patient is prepared as for curettage. After the canal is sufficiently dilated, the radium ring, already loaded with radium, is inserted into the uterine cavity. Because of its flexibility it readily shapes itself within the uterus. The customary rubber tandem sound containing radium (Fig. 7) is then inserted in the uterine canal, and the vagina is packed in the usual manner, thus holding the radium in place.

In some cases the internal cervical os does not dilate readily and may be so rigid as to resist insertion of the ring or, even if this can be forced through, its later removal may be difficult. In such instances the internal os is incised on two

[3] This applicator was made for us by the Radium Chemical Co. of New York City.
[4] Obtained through the courtesy of Hoffmann-La Roche, Inc.

sides with a sharp scalpel, being cut through to a depth of one-eighth inch. Bleeding from this procedure is seldom serious and is readily controlled by the subsequent packing used to hold the radium in place.

Where there is extension of the lesion to the cervix or vagina, additional radium is applied to these involved areas with a colpostat (14), as is customary when primary cervix lesions are treated.

Dosage varies according to the amount of involvement present, 5,000 to 9,000 mg.-hr. (measured in air) being used. In cases where post-radium hysterectomy is planned a 5,000 to 7,000 mg.-hr. dose (measured in air) is sufficient. Where no post-radium operative procedure is to follow, 8,000 to 9,000 mg.-hr. may be administered at one time.

Occasionally there are some complications arising from the radium treatment. Thus, because of involvement by the malignant process the uterine walls may be softened and perforation either with the curette or the radium sound may occur. Usually, however, no serious effect follows, and withdrawal of the radium sound through the gap is sufficient. In the one case in our experience in which this accident did occur no untoward sequelae followed.

In some cases, due to the large amount of radiation given, intestinal disturbances may occur. Diarrhea may be controlled by opiates. Nausea and vomiting may require sedatives and intravenous infusions. Urinary distress may call for catheterization and occasionally intravenous glucose stimulation. In no case have symptoms been severe enough to be alarming or to require removal of radium before the predetermined time had elapsed.

Subsequent treatment depends upon the condition of the patient and the lesion, its extent, and possibility of operation. In those cases where hysterectomy was planned, it was done six to eight weeks after radium therapy. No unusual surgical hazards or difficulties have been encountered by the operating surgeons.

Where treatment was entirely radiological, irradiation in most cases was by high-voltage x-rays through the pelvis, with radium therapy in the uterus and vagina. This latter is used especially in the presence of cervical and parametrial involvement. X-ray therapy is administered in the usual manner through the pelvis and is best given, if possible, prior to radium therapy. When given later it should follow six weeks after radium treatment.

Our series included 101 patients, ranging in age from thirty-three years to eighty-four years. The years of most frequent occurrence were fifty to fifty-two: 10 patients were fifty-two years old, 9 were fifty, 5 were forty-seven years, and 5 were sixty-eight years of age. There were 4 patients each in the forty-two-, forty-six-, fifty-five-, and sixty-year age groups. Other ages were represented by one or two patients each.

In spite of the large colored clientele of this municipal hospital, but 6 cases of uterine cancer in colored patients were referred to us for treatment; all the rest of the series were white women. Only 8 patients were unmarried. The majority of the cases were of an advanced stage when first seen by us.

The most frequent complaint was vaginal bleeding. This was associated in 21 cases with pain; in 13 cases the complaint was discharge and bleeding. Pain varied in intensity, in some cases being severe enough to require rest in bed for relief. Most patients complained of lower back pain. Discharge varied from a brown-colored material to thick bloody pus.

In cases that were not considered totally hopeless, pelvic irradiation usually relieved pain. In advanced cases relief was attempted in some instances by alcohol nerve block.

In all of the 101 cases the clinical diagnosis was cancer, but 5 cases were subsequently proved to be benign, although treatment had already been instituted, mainly for control of bleeding; 1 case appeared to be malignant but was not definitely proved so. In the malignant

group there were 85 carcinomas, 6 epitheliomas, and 4 sarcomas. Of the 6 epitheliomas, 3 were probably originally cancers of the cervix, 11 cases of carcinoma were of undetermined type, and 74 were adenocarcinomas. All these cases were referred for irradiation either because they were too far advanced for surgical handling or because it was hoped that in some instances the local condition would be improved sufficiently following irradiation to warrant operative procedure. During the past four years, however, intrauterine radium therapy has become a regular preoperative measure even in all frankly operable cases.

Of the 95 malignant cases treated, 34 were referred following previous surgery, in most cases hysterectomy; in 61 no operation had been done except diagnostic curettage or biopsy. Sixteen patients were operated upon following irradiation. In 14 of these complete hysterectomy was carried out, in 2 supracervical hysterectomy. Forty-five malignant tumors were treated by irradiation alone, mostly as a palliative measure.

In the group of 34 referred for postoperative irradiation, treatment was by x-ray alone in 21 cases, radium alone in 1 case, and a combination of x-ray and radium in 12 cases. In the preoperative group of 67 cases (benign and malignant) treatment was by x-ray alone in 13, radium alone in 15, x-ray and radium combined in 38; in 1 case, no treatment was given, as the patient died as it was about to be instituted.

In the earlier period of our work, primary operable cases were seldom sent to us for preoperative irradiation, patients being referred for treatment only if the operation did not appear to have been completely satisfactory, or as a precautionary measure. Where the condition was far advanced the patient was referred for irradiation, after biopsy, solely as a palliative measure. In some cases, however, although the disease was in an advanced stage, irradiation was requested with the hope that the local lesion could be so controlled as to make subsequent operation feasible. For these reasons such preoperative and palliative cases were treated in most instances by combined x-ray and radium therapy. In more recent years, as preoperative radium treatment has been recognized as of definite advantage, more and more primary operable cases have been referred for this purpose. In these cases treatment has been carried out with large doses of radium alone. Since 1930 we have been employing this method, applying to the uterine cavity doses of 4,000 to 9,000 mg.-hr. at one time. In most cases this has been done with the tandem or multiple sound method; in 4 cases the Friedman hysterostat was used, and in 3 cases the radium ring. (Cases treated by the author elsewhere by the ring method will be reported in a subsequent paper.)

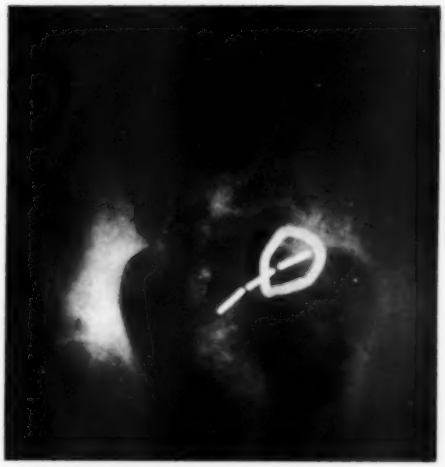

Fig. 7. Radium ring and tandem within the uterus.

This work has been carried on in close co-operation with the gynecological service at Bellevue Hospital,[5] and this friendly arrangement has aided in progressively improving the character of our work and the results achieved.

The results so far obtained with irradiation for cancer of the uterus disclose a definite benefit from this procedure. Nearly all of the uteri removed following

[5] Wm. Studdiford, M.D., Director.

radium treatment have failed to show any residual carcinoma after very careful search. A detailed report of these cases will shortly be made by my associate, Dr. R. Rosh.

Of the 95 patients with malignant tumors treated by all methods, 34 are known to be dead. Death occurred in 1 case before treatment was started, in 23 cases within a year after treatment, in 7 cases between one and two years after treatment, in 2 cases between four and five years, and in 1 case eleven years after treatment.

Of the 35 patients known to be living 7 have lived one year; 4 two years; 7 three years; 5 four years; 1 six years; 2 seven years; 1 eight years; 1 nine years; 1 ten years; 1 eleven years; 1 thirteen years; 1 fourteen years. The 3 cases treated with the radium ring are too recent for a report of results. One of these patients is especially interesting, as she was treated by us with x-ray in 1928 for benign bleeding, proved by biopsy, and has since returned with recurrent bleeding from a carcinoma of the uterus, also proved by biopsy.

Of the 16 patients with malignant tumors who were operated on following irradiation, 9 are dead, one each six, fourteen, fifteen, sixteen, eighteen, and twenty-one months after operation; one two years, one three years and nine months, and one five years after treatment. Seven patients are at present living and well, one seven years and 2 three years after operation. Of the 34 patients treated postoperatively, 12 are known to be dead. Of the 45 treated by irradiation alone, 13 are known to be dead.

CONCLUSION

While surgery is seemingly the best method of treating uterine cancer, irradiation when properly administered, with the newer technics, offers an alternative method giving equally good results.

As a preoperative measure irradiation is a definite adjunct to surgery.

With the newer technics larger doses of radium may be utilized for intrauterine irradiation with safety. Such treatment in no way increases the difficulty of subsequent operative procedure.

As a palliative measure irradiation is definitely beneficial.

A new intrauterine radium device is briefly described.

A general report on 101 cases treated in the Radiation Department of Bellevue Hospital is given.

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DISCUSSION

William E. Costolow, M.D. (Los Angeles, Calif.): Dr. Kaplan has thoroughly analyzed the present-day information regarding the treatment of carcinoma of the corpus uteri. For many years this condition was considered to be entirely a surgical problem, chiefly because it was thought that the percentage of curability was quite high. Thorough study of the world's literature, especially the review by Heyman of Stockholm, demonstrated that the percentage of surgical cures in corpus carcinoma is much lower than had been generally believed. Dr. Kaplan has spoken of the misconception regarding the radioresistance of fundal cancer. Apparently

the low-grade lesions have the best chance of cure, whether treated by surgery or radiation.

We entirely agree that the extent of the disease is the most important factor determining prognosis. If the cases are treated when the disease is in the early stage, results will be good in all histologic types. This is important when it is realized that corpus carcinoma has the best prognosis of any type of cancer which a woman may have, with the exception of skin cancer.

Improvement in intrauterine radium technic has definitely increased the curability of corpus carcinoma. Preoperative irradiation followed by hysterectomy, which lately has been used so extensively in operable cases, is a logical procedure and affords an excellent opportunity for evaluating the effect of radiation therapy. In histologic grades III and IV, a preoperative combination of radium within the uterus and x-ray externally is certainly indicated.

Dr. Kaplan states that "nearly all of the uteri removed following radium treatment have failed to show residual carcinoma after very careful search." This is encouraging but somewhat surprising, as in most series reported in the past, a considerable percentage showed cancer in the uteri removed. If continued work with large series of cases in Dr. Kaplan's clinic and other clinics demonstrates that cancer can be destroyed by preoperative radiation therapy in nearly all cases, then of course radiation will become the method of treatment in carcinoma of the fundus. We feel, however, that until this fact is demonstrated in a large series of cases, the treatment of corpus cancer, in operable cases, should continue to be preoperative irradiation followed by total hysterectomy.

Doctor Kaplan (*closing*): In the uterine cavity we use 0.5 mm. of platinum as a filter. For the cervix we use 2.5 mm. of platinum.

A Study of Radiological Treatment of Cancer of the Cervix[1]

M. C. REINHARD, M.A., H. L. GOLTZ, B.S., and B. F. SCHREINER, M.D., F.A.C.S.
Buffalo, N. Y.

THE FOLLOWING study was made on 557 cases of cancer of the cervix admitted to the State Institute for the Study of Malignant Diseases from 1931 to 1935, inclusive. This number represents all of the cases in clinical groups I, II, and III, which were admitted during this period, the classification being made in accordance with the League of Nations recommendations prior to 1938. No group IV cases are considered in this report. The age distribution at the time of admission is presented graphically in Figure 1, which shows a definite peak at 47.5 years.

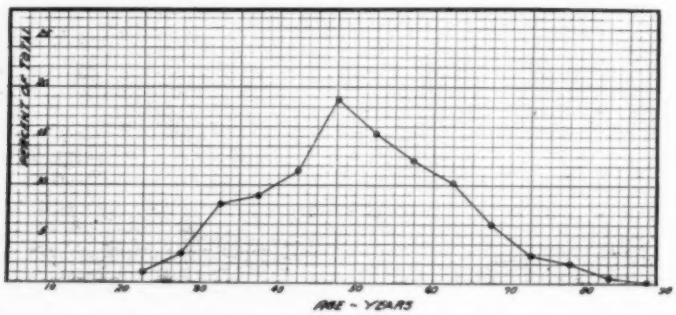

Fig. 1. Age distribution of 557 cases of cancer of the cervix, groups I, II, and III.

The percentage survival curves of each of the three groups (60 in group I, 174 in group II, and 323 in group III) are shown in Figure 2. These curves represent the survival up to five years of all patients, regardless of method of treatment, absence of treatment, previous treatment, death with or without disease. In those cases which were lost, the survival was considered as up to the last visit to the hospital. Because of these inclusions, the five-year end-results are not to be compared with the five-year end-results usually reported under the League of Nations recommendations. While these curves show the percentage survival up to five years, there is no indication of a leveling off at the five-year period and presumably the curves will continue downward with increasing time.

One of the purposes of this study was to associate, if possible, the end-results of radiation therapy with the dosage. It was found that 457 cases fell into two distinct groups on the basis of treatment technics. The remaining 100 cases were eliminated from this study, for one of the following reasons. (*a*) Other radiation technics were used during this period (1931–35), as teleradium therapy or protracted roentgen irradiation with 200 kv. and 0.5 mm. copper filter or Thoraeus filter, with or without interstitial or intracavitary radium. Such a small number of cases, however, were treated by any one of these methods that a study of them would not yield significant results. (*b*) Several cases had received radiation treatment elsewhere prior to admission. (*c*) A few cases received no treatment after admission. (*d*) Death was due to some other cause than cancer.

The 457 cases received radiation ad-

[1] From the State Institute for the Study of Malignant Diseases, Buffalo, New York; Burton T. Simpson, M.D., Director. Accepted for publication in April 1942.

ministered over a period not exceeding four days. This method, hereafter referred to as primary irradiation, consisted in (*a*) one or two small doses of 200 kv. x-rays, having a half-value layer of 0.9 mm. copper, delivered anteriorly and posteriorly through 20 × 20-cm. ports of entry at a target-skin distance of 80 cm.; (*b*) insertion of radium tubes of 100 to 200 mg. radium content, with 1.0 mm. platinum and 1.0 mm. steel filtration, in the uterine canal; (*c*) gold radon seeds, with 0.3 mm. gold filtration, in the cervix and palpable part of the tumor. While this may not represent as satisfactory a procedure as desirable, it was the most expedient method at the time, due to the physical limitations of hospitalization. Of the 457 cases there were 230 which received supplementary irradiation, consisting of protracted irradiation either from radium packs or 200 kv. x-rays, radium tubes and seeds, or any combination of these.

An analysis of the 227 cases receiving primary irradiation only, shows 32 cases in group I, 70 cases in group II, and 125 cases in group III. A similar analysis of the 230 cases receiving supplementary irradiation at a later time, in addition to the primary course of treatment, shows 18 cases in group I, 68 in group II, and 144 in group III. Survival curves for these two groups are shown in Figure 3. For reasons previously stated, the five-year survival as indicated on these curves should not be compared with the usual five-year end-results based on the League of Nations recommendations.

These curves show very definitely that the survival of the patients receiving primary irradiation is much higher than the survival of those receiving a supplementary course at a later date. The marked difference in the curves for the two groups may be due to several factors working individually or in combination. Among these may be included the extent of the disease, the biological variations in both the disease and the patients, the age of the patient, and the supralethal influence of additional radiation.

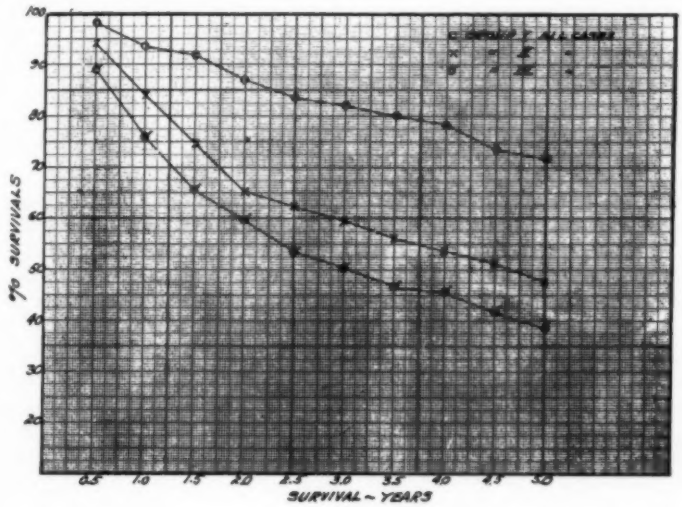

Fig. 2. Survival curves for all cases in groups I, II, and III.

A study of the curves in Figure 3 shows that curve D, representing the survival of group I cases receiving supplementary irradiation in addition to the primary course, coincides very closely with curve B, which shows the survival of group II cases receiving primary irradiation only. Further inspection shows that curve C for group III receiving primary irradiation

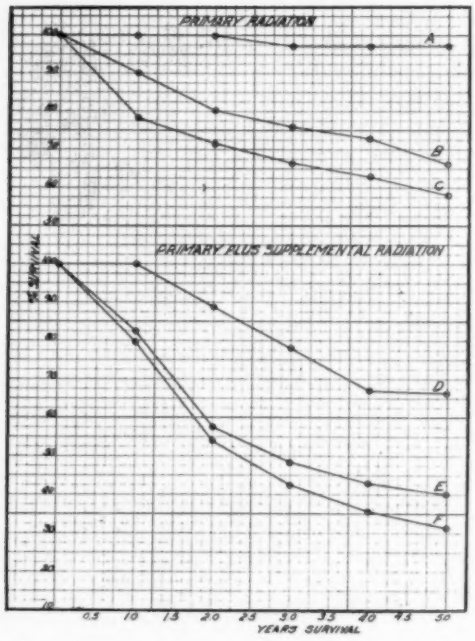

Fig. 3. Survival curves showing (A) group I, 32 cases treated by primary irradiation only; (B) group II, 70 cases with primary irradiation only; (C) group III, 125 cases with primary irradiation only; (D) group I, 18 cases with primary plus supplemental irradiation; (E) group II, 68 cases with primary plus supplemental irradiation; (F) group III, 144 cases, primary plus supplemental irradiation.

only is not much lower than curve D. It would seem, therefore, that curve D represents some cases which may have been more extensive and should have been classified in a more advanced group, or the poorer survival may be attributed in part to the effect of the radiation itself.

It has long been recognized that the effect of radiation on tumors is influenced by a group of factors such as the histology and pathology of the tumor and the physical and physiological condition of the patient, but these factors, particularly the last two, are difficult to evaluate. A review of the microscopic sections of the various tumors from histologic and pathologic points of view failed to show any consistent difference between the cases of the two groups.

In order to determine the influence of age in these two groups of cases, we have plotted the age at admission against the percentage of maximum incidence of the various groups, in Figure 4. It is evident from the curves representing group I cases that there is no marked difference in the age distribution between the two methods. This is not conclusive, however, because of the small sample. For groups II and III there is a marked difference in the age distribution associated with the two meth-

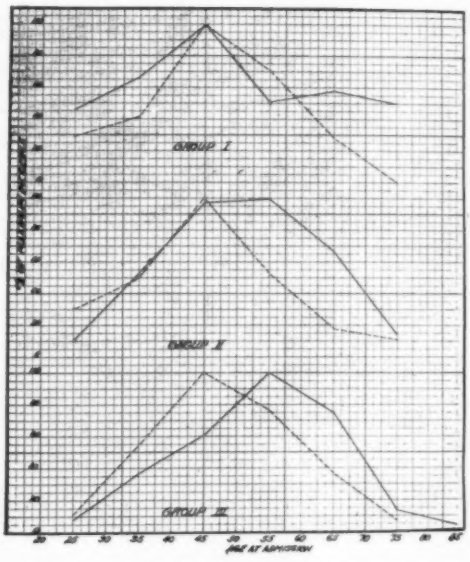

Fig. 4. Age distribution for groups I, II, and III. Solid lines, primary irradiation only. Dotted lines, primary plus supplemental irradiation.

ods of treatment. Those cases which were treated with supplementary radiation at some period following the primary treatment fall into a younger age group; in other words, a better survival is associated with the group in which the tumor occurred at a more advanced age. Inasmuch as many of the patients were elderly, the influence of the normal death rate might be considerable. In order to show this influence and also to demonstrate any difference resulting from the two methods of treatment, all of the 457 cases, regardless of clinical grouping, were combined, the survival was determined for the various age groups and the cases were separated into two sections according to method of treat-

ment. Figure 5 shows the percentage survival for five years against age for each method of treatment as well as the survival curve for all females according to the U. S. census of 1910. The curve representing those cases which received only primary irradiation indicates that the percentage survival increases with increasing age up to fifty-five years before declining, and the survival then follows the normal curve at a somewhat lower level, very nearly reaching the normal curve at the age of seventy-five. On the other hand, the curve representing the second method of treatment, *i.e.*, a supplemental course or courses following primary treatment, shows no improvement in survival up to the fifty-five-year period, although from sixty-five onward the influence of the normal death rate is apparent.

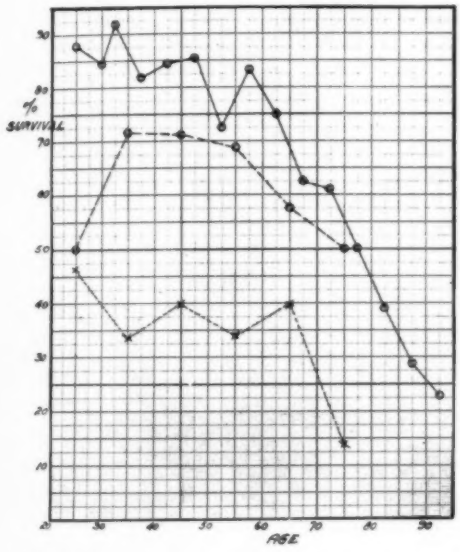

Fig. 5. Percentage of five-year survivals for various ages. O-------O 227 cases groups I, II, and III, primary irradiation only. ×-------× 230 cases groups I, II, and III, primary irradiation plus supplemental irradiation. O———O All classes of females, U. S. Census 1910.

In an endeavor to associate end-results with the amounts of radiation administered to various points in the pelvis, dosages were summated from x-ray, radium tubes, and seeds to points 2, 3, and 5 cm. lateral to the mid-line. The average dose delivered to the three points by the primary irradiation only, in the three clinical groups, is shown in Figure 6. A steep dosage gradient with distance is shown in all three curves and it can be observed that the average dose in group III cases is not materially greater than for the other two groups, particularly at the 5-cm. mark, which may be a probable point of extension of the disease in group III. The summation of dosages in roentgens received by the various points from both radium and x-rays is not satisfactory and is open to criticism because of the relative biological efficiency of the radium roentgen as compared with the 200-kv. x-ray roentgen. This problem is made still more difficult by the change in wavelength of both gamma rays of radium and the x-rays with the amount of tissue irradiated. However, the sum of the dosages delivered to the 2-cm. point was composed almost entirely of radium roentgens, while at the point 5 cm. from the mid-line, the ratio of radium to x-ray roentgens was of the order 2:1.

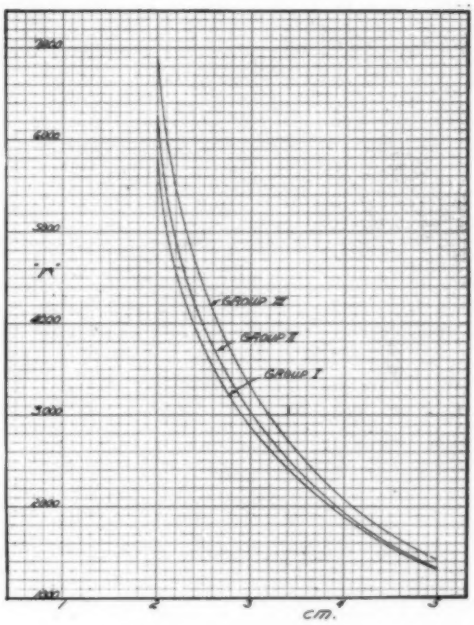

Fig. 6. Curves showing the average doses delivered by radium tubes and radon seeds lateral to the mid-line of the pelvis.

A typical isodose chart for combined radium tubes and seeds is shown in Figure 7, where the radon seeds are centered around the lower quarter of the radium tubes in the cervix. This is an ideal set-up and is rarely obtained practically. For purposes of calculation of dosages at various points in the pelvis, however, charts of this type were used. Allowance was made for any variation in the length of the radium tubes. According to Tod and Meredith (1) and Tod (2), the limit of tolerance to treatment by intracavitary radium is not determined by the dose on the vaginal surface but by a zone of tissue which they called the paracervical triangle, which extends to about 2 cm. lateral to the mid-line. In the following table, therefore, we have considered only the dosage delivered to the 2-cm. point.

Since there were relatively few group I cases, it was decided to consider groups I and II together. The distribution of cases for the two treatment methods, whether the patients were alive and well or dead at the end of the five-year period, is shown in Table I. The dosage bracket 4,000–5,000 r includes a few patients who received less than 4,000 r and similarly the 7,000–8,000 r bracket includes a few patients who

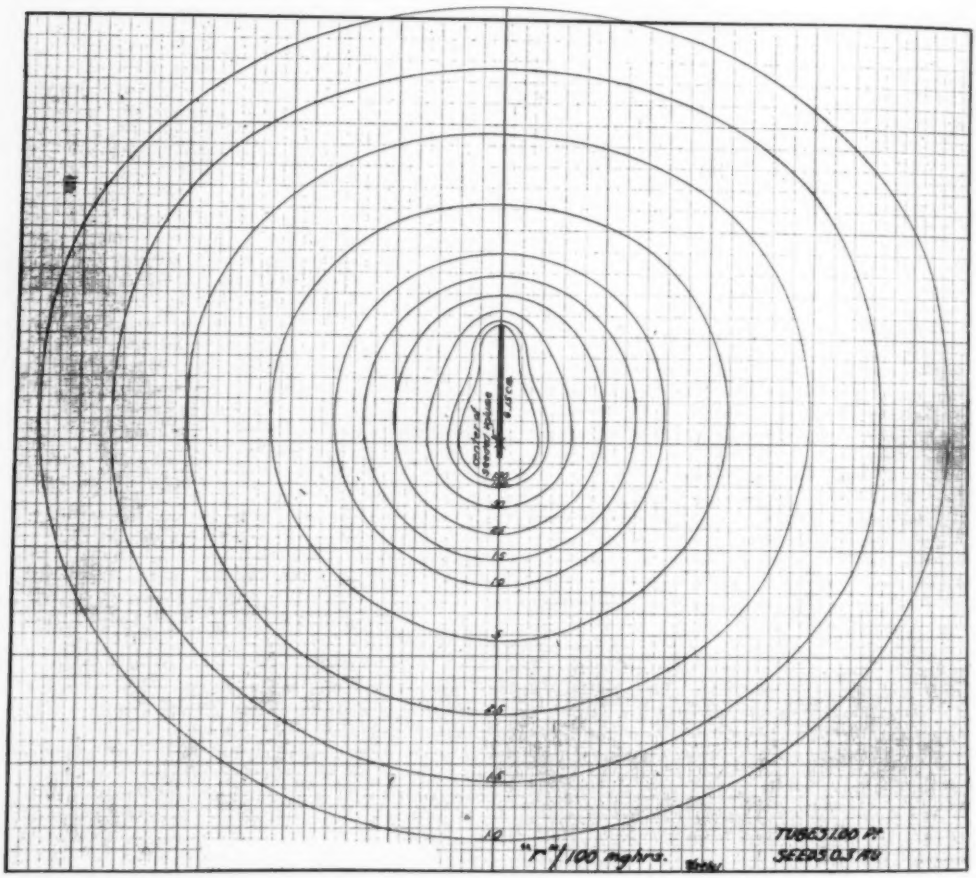

Fig. 7. Isodose chart for radium tubes 6.15 cm. active length and radon seeds placed centrally around the lower quarter of the radium tube; based on equal quantities of radium and radon.

TABLE I: RESULTS OF TREATMENT IN CERVICAL CANCER

	Groups I and II				Group III			
	Primary Irradiation				Primary Irradiation			
Dose	4–5,000 r	5–6,000 r	6–7,000 r	7–8,000 r	4–5,000 r	5–6,000 r	6–7,000 r	7–8,000 r
No. alive and well	14	22	30	12	4	12	31	25
No. dead	4	6	10	4	3	9	19	22
Total	18	28	40	16	7	21	50	47
Percentage alive and well	77.8	78.4	75.0	75.0	57.2	57.2	62.0	53.2
	Primary Plus Supplementary Irradiation				Primary Plus Supplementary Irradiation			
No. alive and well	4	6	12	13	1	7	13	14
No. dead	4	16	17	14	3	16	41	49
Total	8	22	29	27	4	23	54	63
	Summary				Summary			
Alive and well Primary only	14	22	30	12	4	12	31	25
Grand total	26	50	69	43	11	44	104	110
Percentage failures	46.2	56.0	56.5	72.0	63.8	73.0	70.0	68.0

received slightly more than 8,000 r. It can be noted that with primary irradiation the percentage survival remains fairly constant at about 75 per cent for groups I and II and it can be concluded that dosages of the range shown are adequate in about 75 per cent of these cases. On the other hand, for the dosage range shown in the table, there is apparently no improvement in end-results with the higher doses. In the remaining 25 per cent of these cases, it is reasonable to suppose that one of the possible causes for the failure of the treatment might be the extension of the disease to a region where the dose was inadequate.

In tabulating those cases which received supplementary treatment in addition to the primary course, the actual doses recorded are from the primary irradiation only. Dosages delivered by the supplemental irradiation have not been included in this chart. Although it is apparent that a certain percentage of the patients who received supplementary irradiation are free from disease at the end of five years, nevertheless we have considered the necessity for supplemental irradiation as the failure of the primary irradiation to control the disease. If we add these failures to those of the group receiving primary irradiation only who died of the disease, we can estimate the total percentage failure in groups I and II. These percentages are included in the lower portion of the table and show a tendency toward an increase with increasing dosages. This again calls to mind the possibility of under-estimation of the extent of the disease as well as the possibility that the supplementary irradiation may have contributed to the fatal outcome.

A survey of the magnitude of the supplementary irradiation, which for the most part was protracted irradiation of the entire pelvis and was usually given within the first year following primary irradiation, shows that approximately 50 per cent of 86 cases received less than 2,000 r additional dosage at the 2-cm. point, and of these 54 per cent have remained well for at least five years. On the other hand, those cases receiving more than 2,000 r supplementary radiation at this point showed only a 29.8 per cent survival.

There were 125 cases in group III treated by primary irradiation; the dosages for these cases were also estimated to a point 2 cm. lateral to the mid-line, although this point does not necessarily represent the spread of the disease. The results of these calculations are also presented in Table I. Here again there is no indication of a better survival with higher doses within the range of 4,000–8,000 r. Instead, within the dosage range mentioned, the percentage survival is fairly constant at about 55 per cent for all the dosage brackets. The addition to this

table of the cases receiving supplementary irradiation, shows that, unlike groups I and II, the percentage of failures does not increase with the larger doses.

When we consider the supplemental irradiation administered to group III patients, we note that here as in the group I and II cases the supplemental irradiation was largely protracted roentgen irradiation to the entire pelvis, and also that there were 50 per cent of the 144 cases which received less than 2,000 r within the first year following the primary course of treatment. Of these, 31 per cent remained well for the five-year interval, whereas in all the remaining cases receiving more than 2,000 r supplemental radiation, the survival is only 17 per cent.

SUMMARY

This study includes graphs showing the age distribution and survival of 557 patients with cervical cancer of clinical groups I, II, and III, regardless of treatment, admitted to the State Institute for the Study of Malignant Diseases from 1931 to 1935, inclusive. Of the 557 cases, 457 were classified according to treatment into two groups: those receiving primary irradiation only and those receiving primary plus supplemental irradiation. Approximately 50 per cent of the 457 cases required retreatment and fell into the second group. The survival rate for this group is definitely less than for the cases receiving primary irradiation. The poorer survival of this group could be attributed to one or more of the following causes: (*a*) the nature of the disease itself, (*b*) extension of the disease to regions of inadequate dosage, (*c*) the normal biological variation among individuals, (*d*) the supralethal effect of the radiation, (*e*) the age of the patient.

The age distribution of these two groups is shown graphically. From the curves it is obvious that a better survival is associated with the older age groups. Curves are also included which show the influence of age on the percentage survival of the two groups mentioned as well as the normal expectancy of life in a female population.

Isodose and dosage distribution curves are presented. The average dosage curves show a steep gradient, from 2 to 5 cm. lateral to the mid-line, which is reflected in the progressively poorer survival with increased spread of the disease.

Doses at the 2-cm. mark, within a range of 4,000 to 8,000 r primary radiation only, were capable of producing a 75 per cent five-year survival free from disease in the combined I and II groups, and a 55 per cent five-year survival free from disease in the group III cases.

Because of the poorer survival of group III cases, where the disease has presumably spread to regions receiving lower doses, it would seem reasonable to conclude that the dosage to the lateral portions of the pelvis should have been increased.

Of those patients in groups I, II, and III receiving supplemental irradiation, the highest survival is associated with doses less than 2,000 r in addition to a full course of primary irradiation.

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Diseases of the Lesser Circulation[1]

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REGULATION OF the lesser circulation differs primarily from that of the greater circulation in four ways:

1. The chemical and nervous control of the caliber of the small pulmonary vessels, though it exists, is of secondary importance in regulating blood flow through the lungs. Such control is of primary significance in the greater circulation because of the need to shunt blood from a resting to an active organ.

2. The pulmonary arterioles have six to eight times the diameter of the greater circuit arterioles, and the lung capillaries also are very wide. Thus, when congestion occurs, a large volume of blood can accumulate in the lungs.

3. The volume of blood flowing through the lungs in health depends primarily on the activity of the heart and not on resistance in the lungs.

4. Under conditions of stress the left ventricle is able to pump more blood than the right ventricle. Since its vessels are larger and more passive, the pulmonary blood flow is regulated chiefly by the work of the heart. Because of its position as a relatively passive circuit between two forces, the pulmonary circuit is more subject to large unexpected increases in pressure.

The most important abnormal condition in the lesser circulation is hypertension. This must result from some defect in the circulation, causing backing up of blood in the pulmonary circuit, combined with a relatively efficient right ventricle. The old "forward" heart failure theory of Mackenzie has been generally discarded and it is now agreed that the common mechanism is backward failure. Thus, for example, if the left ventricle fails it is unable to expel as much blood as has been delivered to it, and after it dilates the blood backs up into the pulmonary bed. If the right heart succeeds in beating effectively against this increased work, pulmonary hypertension results. Occasionally, the right ventricle fails simultaneously, in which event no pulmonary hypertension results. Because of the large potential diameter of the pulmonary capillaries, pulmonary hypertension is usually associated with pulmonary engorgement.

This concept is important to the roentgenologist because it explains the variability in lung appearances in the common types of heart lesion. It also draws attention to the fact that before pulmonary hypertension with its associated dyspnea and other manifestations can occur, the heart must be enlarged (except in some cases of constrictive pericarditis). It explains the increased density and size of the hilus shadows, increased lung markings, and the radio-opaque appearance of the lung fields proper.

Diseases of the Lesser Circulation Characterized by Pulmonary Engorgement: The most common cause of pulmonary hypertension and engorgement is left ventricular failure. This is due most frequently to hypertensive heart disease and less commonly to myocardial infarction, aortic regurgitation, and aortic stenosis. Rheumatic mitral valvulitis with predominant stenosis is another important cause of pulmonary engorgement. Congenital heart lesions result in pulmonary engorgement if an important shunt exists between the left and the right heart. The higher left heart pressure results in abnormal blood flow to the right heart. A widely patent ductus arteriosus and interauricular septal defects are the common examples. Left-to-right heart shunts are rarely caused by

[1] From the Department of Medicine of the University of California Medical School, San Francisco, Calif. Presented before the Radiological Society of North America at the Twenty-seventh Annual Meeting, San Francisco, Dec. 1–5, 1941.

traumatic or syphilitic arteriovenous aneurysms. If large enough and/or close enough to the heart, these may result in pulmonary engorgement.

The diseases characterized by pulmonary engorgement have in common some or all of the following clinical findings: dyspnea; slight cyanosis; a loud pulmonary second sound; basal râles; occasionally a basal gallop; an electrocardiogram with a right axis shift, a Q3, an S1, and often depression of S-T2,3 and low or inverted T2, T3, T4; a heart shadow with a prominent pulmonary conus, increased density and size of hilus shadows; increased lung markings; often a more radio-opaque appearance of the lung fields proper.

Diseases of the Lesser Circulation Characterized by Intrinsic or Extrinsic Blocking of the Pulmonary Vessels: This less important group of diseases has occasionally been referred to as primary cor pulmonale or the pulmonary hypotension group. The location of the obstruction will determine largely the extent of pulmonary bed with blocked blood supply. Thus, pulmonary vein obstruction will result in engorgement of the extensive proximal pulmonary bed and result in a different clinical picture from obstruction in the main branches of the pulmonary artery.

The most important of this group of diseases is massive pulmonary embolism, the cause of about 5 per cent of all heart failure, and now commonly called acute cor pulmonale. A rare subgroup, designated subacute cor pulmonale, is due to an unusual type of diffuse lung metastasis which, in the course of a few days or weeks, blocks the pulmonary blood flow. Of the few cases reported nearly all have been in patients less than forty years of age, usually with carcinoma of the stomach or, occasionally, of the colon. A third subgroup commonly called chronic cor pulmonale, makes up about one per cent of organic heart disease. It includes extensive pulmonary fibrosis, emphysema, and pulmonary vessel obstruction due to other less common causes, such as chest deformities, primary pulmonary artery or arteriolar disease, schistosomiasis, and tracheal or bronchial stenosis.

The clinical manifestations in the three types of primary cor pulmonale may differ from those of the pulmonary hypertension group, due to the relative absence of pulmonary engorgement in the former. Thus, râles may be absent and the lung fields may be unusually radiolucent. Underlying lung disease, however, often adds confusion. Cyanosis is usually more marked, and in the chronic types (especially with pulmonary fibrosis and emphysema) the fingers and toes may become clubbed and polycythemia may develop.

SUMMARY

An understanding of the diseases of the lesser circulation requires knowledge of its physiological and anatomical differences from the greater circulation.

Pulmonary hypertension or engorgement are most commonly due to left ventricular failure, mitral stenosis, and congenital, traumatic, or syphilitic left-to-right heart shunts.

Disease of the lesser circulation characterized by intrinsic or extrinsic obstruction of the pulmonary vessels (cor pulmonale) has many clinical similarities to the group with pulmonary hypertension, since right heart strain is common to both.

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Faulty Movements of the Diaphragm as a Cause of Non-Obstructive Emphysema and Angina Pectoris[1]

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IN PREVIOUS papers (1) we have discussed the postural syndrome which begins with obesity and results in distortion of the spinal curves. Distortion of the spinal axis leads to many other complications which are of interest to the roentgenologist but beyond the scope of this report.

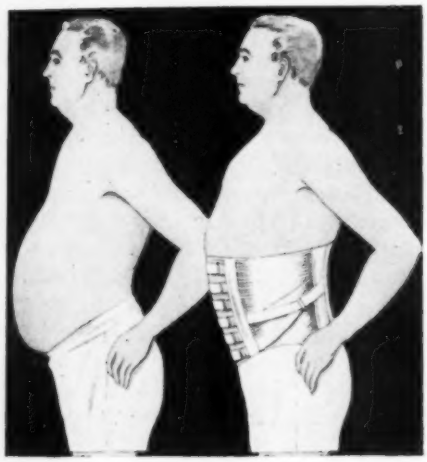

Fig. 1. Appearance of patient with the postural syndrome (with obesity, increased spinal curves, postural emphysema, radiculitis, and other complications) before and after application of a suitable belt.

For many years we have seen patients who complained of dyspnea and cough and who had been referred because of suspected myocardial failure. Upon close questioning it was found that the dyspnea came on only in the upright posture. The patients were able to sleep without extra pillows. The cough also was more troublesome in the upright position. Most of these patients were obese. Upon examination the lungs were found to be markedly emphysematous. In the past most clinicians have diagnosed the pulmonary condition as chronic bronchitis and emphysema or as asthmatic bronchitis. The *orthostatic* dyspnea was shown to be of pulmonary origin. The emphysema was demonstrated to be the result of increased volume of the chest. Previous writers (2) have designated this non-obstructive emphysema as the senile type to distinguish it from the obstructive emphysema seen in bronchial asthma and from other types of obstruction of the airways. Kountz and Alexander recommended the use of a firm supporting belt to hold up the pendulous abdomen and to aid in the diaphragmatic movements. We modified this belt by adding elastic segments at the sides (Fig. 1) to insure freer motions of the diaphragm (3).

The treatment of patients with so-called chronic bronchitis with emphysema has been remarkably successful. The orthostatic dyspnea and cough are promptly relieved. A dietary régime is then instituted, which aids further in restitution of a more normal functional state. Some of our earlier experiences with this group of patients suggested new avenues for the study of a closely related syndrome designated as angina pectoris. The patients who had been treated for pulmonary symptoms occasionally mentioned that a sensation of substernal compression with radiation to the left arm, to the neck, or to other areas, which had come on with exercise, had been relieved after they began to wear the elastic supporting belt. Further intensive study showed that a very large proportion of the patients whose chief symptom was anginal pain could be relieved by similar methods of treatment. Our experience covers a period

[1] From the Department of Medicine, University of California Medical School, San Francisco. Read before the Radiological Society of North America, at the Twenty-seventh Annual Meeting, San Francisco, Calif., Dec. 1–5, 1941.

of over five years and is based upon a study of over 300 cases. It is apparent that not only the heart but also the brain and other important organs are affected; however, any further reference to these other structures will be omitted from this report.

The type of person who presents this syndrome (4, 5, 6, 7) almost invariably shows girdle-obesity or has a relaxed abdominal wall. In the obese the protuberant abdomen shifts the spinal axis forward. The upper thorax is displaced backward and the head is moved forward. The cervical and lumbar lordosis is increased and the upper thoracic spine shows a kyphos of varying degree. The strain on the spinous attachments results in local changes in the vertebral bodies. Irritation of nerve roots results in the production of radicular symptoms.

The supporting fascial sheath which extends from the mandible through the cervical fascia, the pericardium, and the diaphragm are relaxed and lose part of their function in respiratory movements. The upper ribs are collapsed in front and the lower ribs are flared and raised as in the inspiratory position. The diaphragm is partially flattened by the outward displacement of the lower ribs and is held down by the weight of the suspended fat on the omentum, mesentery, and abdominal organs. When the patient is in the erect posture, this counterweight interferes with the upward movement of the diaphragm during expiration and in time probably destroys the power of the elastic tissue of the lungs which under normal conditions is the chief means of bringing them back to the collapsed state.

In angina pectoris other factors are of contributory importance (8). The reciprocal changes in pressure between the pleural and peritoneal cavities, brought about by the movements of the diaphragm and the intermittent contraction and relaxation of the muscular bundles of the diaphragm at the point where the inferior vena cava passes through, combine to act as a substation or pumping plant which aids in the return of blood to the heart. In the type of patient described this function is disturbed in the erect posture. From studies on circulation time and blood pressure, and from observations made of patients in different postures with and without an elastic abdominal support, it seems clear that the blood does not return normally to the heart in the erect posture unless the belt is used. It follows that if the blood does not get back to the heart, the heart cannot put out the normal amount. If the output is diminished, the flow to the coronary vessels is reduced. Under such circumstances the area of the heart which is deprived of normal circulation because of sclerosed vessels will be the first to suffer. If the return of blood to the heart is facilitated, the ultimate flow to the coronary arteries may be increased so that the area with low oxygen rations will secure a more adequate supply and symptoms will be averted.

In the roentgen examination of patients it is necessary to keep the foregoing explanation in mind. The patient should be examined in both the erect and the supine position. In the erect posture, when all tight abdominal supports are removed, the diaphragm stands at a very low position. There is generally a widening or flaring of the lower ribs and the diaphragm appears flattened. Forced respiratory movements should not be considered as an indication of the customary respiratory excursion. We know that the vital capacity of these patients is not altered until the last years of life. An estimation of the ordinary respiratory movement (tidal air) is more important. If the patient is placed in the supine position, the diaphragm at rest stands at a higher position, is more convex, and moves through a greater distance. A similar situation may be observed when a properly fitted belt is worn, even when the patient is in the erect posture (Fig. 2).

The shape and position of the heart are altered by the use of the elastic supporting belt. We believe also that the pulsations of the ventricular wall are more vigorous when the belt is worn. Tests for cardiac

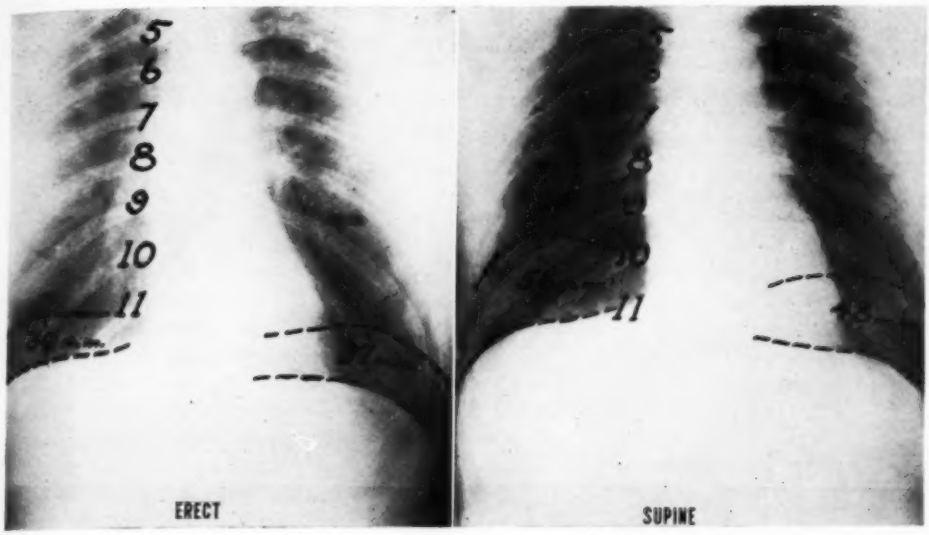

Fig. 2. Roentgen exposure (left) made in the erect posture without a belt, showing the low position of the diaphragm in expiration and the reduced excursion with inspiration, and roentgen exposure (right) showing the position and movement of the diaphragm in the same patient in the supine position. The latter relationships are found in the erect posture also if an elastic supporting abdominal belt is worn. The position of the diaphragm on the original films has been marked for identification. A double exposure was made in inspiration and expiration.

output, however, which are unreliable under even the best conditions, do not show consistent findings. Roentgen kymograms may give false readings if the heart is displaced and perhaps rotated by the application of pressure below the diaphragm. Further study is necessary to clear up some of the factors involved in cardiac output.

The explanation of the benefits derived by patients with senile or non-obstructive emphysema or angina pectoris and allied disorders from the use of an elastic supporting abdominal belt may require further revision. The observation that such patients fall into a well defined group with obesity or visceroptosis, increase in the spinal curves, emphysema, cough, anginal pain, and cerebral symptoms, can be confirmed daily in the office and at the bedside. The physical findings and diagnostic tests show almost uniform abnormalities which indicate faulty movements of the diaphragm. Treatment directed toward restoration of the function of the diaphragm has given results far better than those obtained by any other method of treatment now employed for this group of symptoms. Dietary management and finally postural exercises complete the triad of therapeutic aids.

SUMMARY

The syndrome of obesity, postural emphysema, orthostatic dyspnea, and angina pectoris has been discussed. The importance of the loss of function of the diaphragm in the production of the symptoms has been stated. The use of an elastic supporting abdominal belt, acting as a means of artificial respiration, aids in the restoration of diaphragmatic function. Relief is prompt and spectacular.

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Studies of the Pulmonary Vessels by Means of Body-Section Radiography[1]

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When we were asked to participate in this symposium on the lesser circulation, we were a little reluctant to do so for two reasons: first because we knew so little about the matter, and second because we could recall only a few instances in which we had been able to make a roentgenologic diagnosis of any clinical importance regarding the pulmonary circulation. When we began to study this problem consciously, however, and tried to visualize adequately by body-section radiography the conus arteriosus and the pulmonary arteries and veins, we soon realized that here was a technic by which we could not only study these structures to better advantage, but could also demonstrate segments of them that were not apparent on the conventional films.

Many investigators have written on various methods for demonstrating the pulmonary arteries. Sussman (1) emphasized the importance of the oblique as well as the postero-anterior view. Parkinson and Hoyle (2) and Rubin (3) have done likewise. Robb and Steinberg (4) have contributed a great deal to the study of the lesser circulation by using 70 per cent diodrast intravenously for opacification of the pulmonary vessels, but this method is not always convenient or advisable. Very little has ever been written about the size, shape, position, and course of the pulmonary vessels as seen in the lateral projection. This is understandable, because in the conventional lateral film the shadow of a part of the parent pulmonary artery and shadows of the right and left branches are superimposed. The resulting picture is so complex and poorly defined that it is difficult to identify the separate divisions. For the same reason it is even more difficult to recognize the smaller and less conspicuous pulmonary veins. Body-section radiography gives us the means for visualizing separately either the right or the left pulmonary vessels in cross-section.

ANATOMY

In order to interpret the sectional films, we found it necessary to familiarize ourselves with the anatomy of the lesser circulation, particularly the pulmonary artery and its relationship to the neighboring structures. This is important, since the pulmonary artery is readily identified on the lateral sectional films and, by using it as a bearing point, the neighboring structures can more easily be recognized.

To avoid confusion in the discussion of the anatomy of the lesser circulation we shall follow the terminology advocated by the BNA. Figure 1 is a photograph of the heart as pictured in Sobotta's *Atlas and Textbook of Human Anatomy* (5). The right ventricle forms the anterior and middle third of the heart. The upper and anterior portion of the right ventricle is the *conus arteriosus*, sometimes referred to as the pulmonary conus. It is to be noted particularly that it is a part of the right ventricle and constitutes the outflow tract that leads to the pulmonary artery. Contrary to the diagrams occasionally seen in some reference books, the normal conus arteriosus does not form any part of the cardiac silhouette in the postero-anterior view. The pulmonary arc, as shown by Robb and Steinberg (4), is produced by the pulmonary artery and its left branch. With enlargement of the right ventricle the conus arteriosus enlarges simultaneously and pushes upward and to the left, but not sufficiently to form a recognizable

[1] From the Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine, Saint Louis, Mo. Read before the Radiological Society of North America, at the Twenty-seventh Annual Meeting, San Francisco, Calif., Dec. 1–5, 1941.

bulge on the left border of the heart. As a rule, films must be made in the right anterior oblique and in the left lateral projections to detect even moderate enlargement of the conus arteriosus. Since the conus arteriosus is a part of the right ventricle, enlargement of the conus means enlargement of the ventricle. The roentgenological demonstration of a large conus arteriosus is one of the best means of diagnosing right ventricular enlargement.

The pulmonary artery differs from all other arteries in the body in that it contains venous blood. It arises from the conus arteriosus as a short, thick trunk and extends upward, but mainly backward toward the left border of the spine. It runs about two inches within the pericardium before dividing into a right and a left branch, which pass to the right and left lungs, respectively.

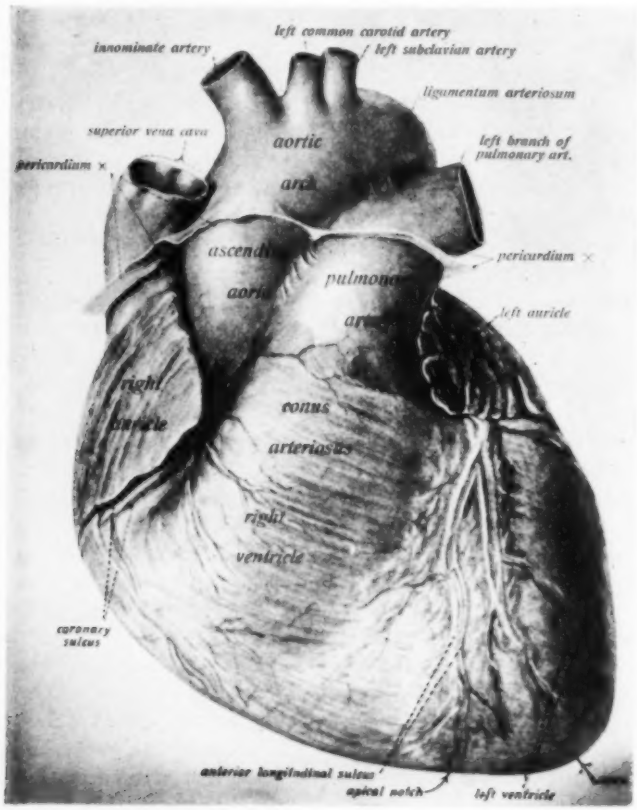

Fig. 1. Drawing of human heart, from Sobotta's *Atlas and Textbook of Human Anatomy.*

This drawing shows that the right ventricle forms the anterior and middle thirds of the heart. The conus arteriosus is a part of the right ventricle and forms the outflow tract that leads to the pulmonary artery. The conus arteriosus is never visualized in the anteroposterior view but must be viewed in the right anterior oblique position. The parent pulmonary artery and the left branch form the pulmonary arc on the left border of the cardiac silhouette. Note that most of the pulmonary artery is covered with pericardium.

The drawing in Figure 2 is taken from Spalteholz's *Hand Atlas of Human Anatomy* (6) to show the course and relationship of the right and left branches of the pulmonary artery. To demonstrate these

relationships, segments of the pulmonary artery, of the ascending aorta, and of the superior vena cava have been removed.

The right pulmonary artery runs to the root of the right lung, where it divides into three branches, one for each lobe. In its course it passes behind the ascending aorta and the superior vena cava, both of which have been removed in this drawing. Behind the right pulmonary artery is the right main bronchus. Above it is the arch of the aorta and below it is the left auricle. Note particularly that at the root of the lung the right pulmonary vein lies anterior to the artery; the right bronchus lies above and posteriorly to it.

The left pulmonary artery is shorter, slightly smaller, and passes in front of the descending aorta to the root of the left lung, where it divides into two branches to supply the upper and lower lobes (Fig. 2). At the root of the lung the left pulmonary artery is uppermost. The left bronchus is below and behind the artery. The left

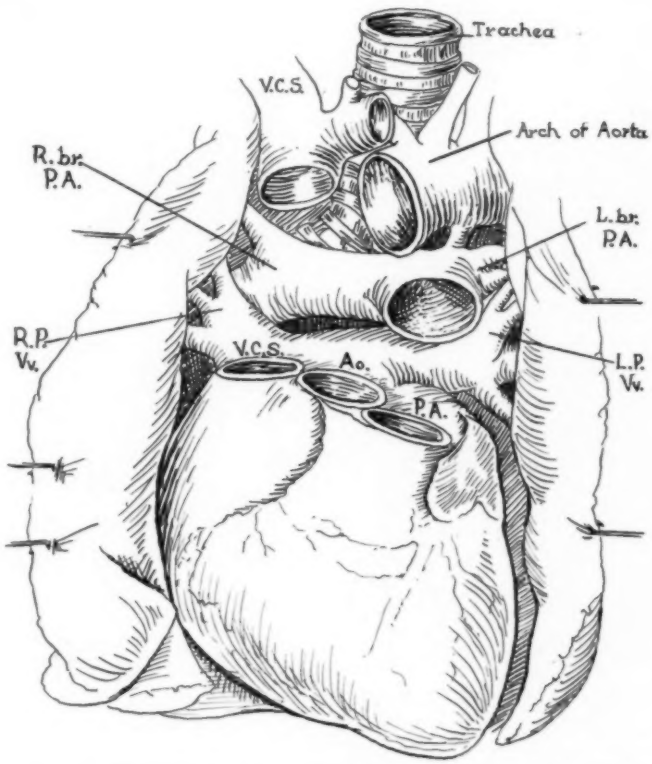

Fig. 2. Diagrammatic tracing showing relationship of pulmonary arteries to pulmonary veins and bronchi, modified from drawing in Spalteholz's *Hand Atlas of Human Anatomy*.

Large segments of the pulmonary artery, the ascending aorta, and the superior vena cava have been removed to permit better visualization of the pulmonary vessels and the bronchi.

The parent pulmonary artery runs slightly upward and posteriorly before bifurcating. The left pulmonary artery is short and runs almost directly posteriorly, as will be shown in the sectional films. At the lung root the left pulmonary artery lies cephalad to the left pulmonary vein and anterior to the left bronchus.

The right pulmonary artery is longer and runs laterally several inches before reaching the lung root. The artery is cephalad to the right pulmonary vein and anterior to the right bronchus.

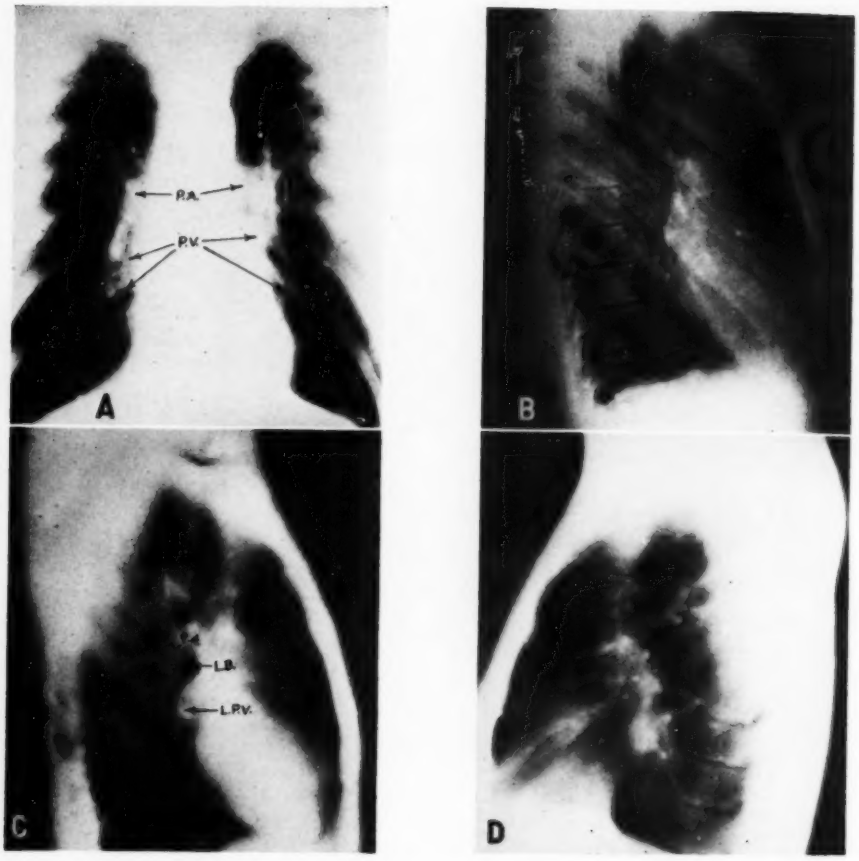

Fig. 3. Pulmonary arteries and veins as visualized by sectional radiography in a healthy adult.

A. Postero-anterior sectional film of pulmonary vessels. This is the least satisfactory position for visualizing the pulmonary arteries (P.A.), which are the group of vessels that lie cephalad. As a rule they are the larger vessels and form the bulk of the pulmonary vessels at the hilus.

The pulmonary veins (P.V.) are more difficult to demonstrate, as they are smaller, and the main trunks that enter the auricles are very short and thus do not provide sufficient contrast in density to permit their recognition. The pulmonary veins are the smaller trunks that lie caudad to the arteries.

B. Lateral conventional film of chest. Conventional films made in this position are of little value in studying the pulmonary vessels, as all those on the right and left sides are superimposed, and the resulting shadows are too complicated for accurate interpretation.

C. Lateral sectional film of left pulmonary vessels (section 10 cm. medial from lateral chest wall). The left pulmonary artery (L.P.A.) runs upward, then posteriorly, and finally caudad. It forms a semicircular ring about the left main bronchus (L.B.). The left pulmonary vein (L.P.V.) is the oval shadow just in front and below the bronchus. Compare the clarity with which the pulmonary vessels are displayed on the sectional film with that shown on the lateral conventional film.

D. Lateral sectional film of right pulmonary vessels (section 10 cm. medial from lateral chest wall). The right pulmonary artery is not so easily demonstrated as the left, because the main trunk ends abruptly at the lung root by dividing into many more divisions than is the case with the left pulmonary artery. Thus in most instances two different views can be obtained of the right pulmonary artery. One view can be made through the main trunk, which appears as a large oval shadow, as shown in Figure 7-D. The second view, as shown here, can be made at the level of the lung root, showing the many branches of the artery as it spreads throughout the lung. The right pulmonary veins are not seen, as they lie a few centimeters medial to this level.

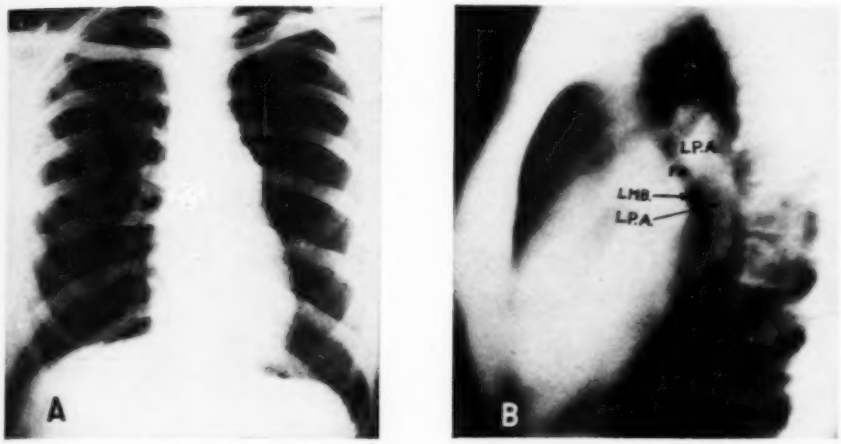

Fig. 4. A prominent pulmonary arc is shown to considerable advantage in the left lateral sectional film, which should be employed in the study of abnormal shadows in this area.

A. Postero-anterior chest film of an adult woman. The prominent bulge of the pulmonary arc was sufficient to warrant further roentgenologic studies.

B. Lateral sectional film through the left pulmonary arc. A short segment of the parent pulmonary artery (P.A.) is seen through the left main bronchus (L.M.B.), which just overlies it. The left pulmonary artery (L.P.A.) is oval-shaped with the largest branch running downward and slightly posteriorly.

pulmonary vein lies in front of the artery.

It should be pointed out that the walls of the pulmonary arteries are thinner than those of the aorta. This fact may explain in part why these vessels are nearly always enlarged and dilated in diseases that involve the pulmonary circulation.

TECHNIC

Bearing these anatomical facts in mind we proceeded to see how clearly these structures could be demonstrated by sectional radiography in patients with and without abnormal changes in the pulmonary circulation. Conventional films were made first on each patient in the postero-anterior, in the right and left anterior oblique, and in the left lateral positions. By analyzing the location of the pulmonary vessels as seen on the conventional films, it was possible to determine the approximate levels in the various positions in which the sectional films were to be made. This method served two purposes: first, it provided a set of the conventional films and a set of the sectional films of the pulmonary vessels for comparison; second, it prevented the needless exposure of a large number of films in the attempt to depict the proper level.

The laminagraph of Kieffer and Moore was used for taking the sectional films and proved highly satisfactory. This equipment produces a complete blurring of the unwanted structures and in that way provides a uniform background. The principles of body-section radiography have been published so often (7, 8, 9) that no discussion of this problem will be considered here. The spiral motion was employed throughout in order to gain the maximum blurring of unwanted shadows. The four-second exposure was not appreciably objectionable, as the object of the study was to obtain better visualization of the large pulmonary vessels and we were not particularly concerned about the detail of small and delicate vessels. Between 200 and 300 milliampere-seconds were used during the exposures to gain the greatest amount of contrast. This is important, as the large pulmonary vessels are in such intimate contact with structures of approximately the same density that it is at times difficult to separate them, under the best circumstances. The anteroposterior, the lateral,

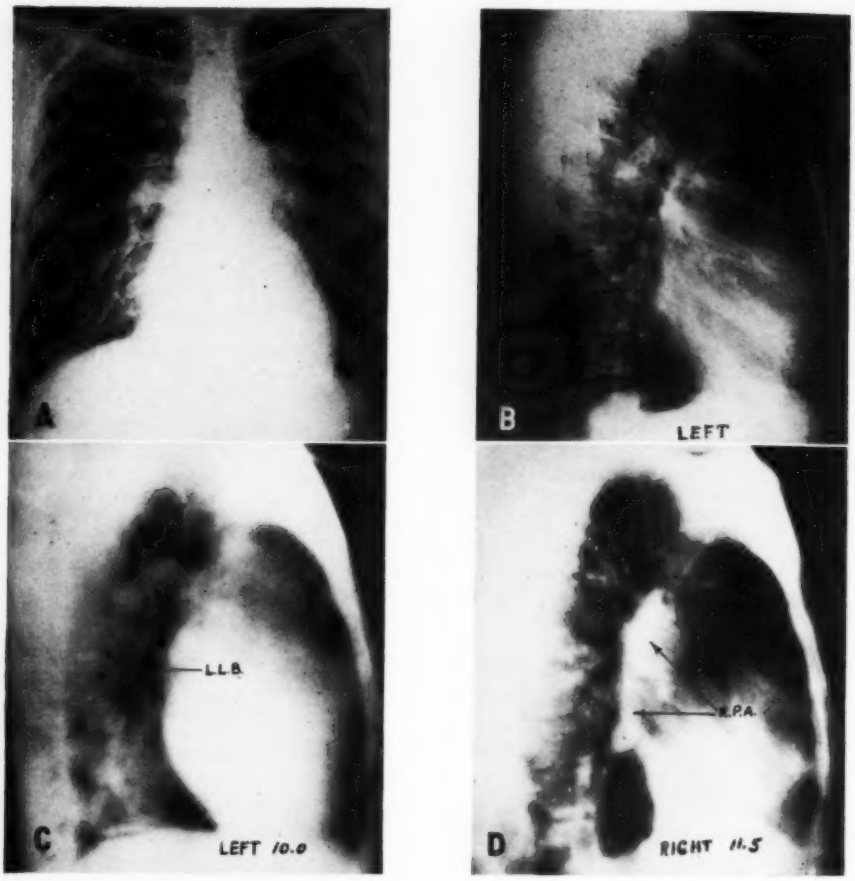

Fig. 5. Enlarged and dilated pulmonary vessels in a 33-year-old man with a patent ductus arteriosus.

A. Conventional postero-anterior chest film. Note the prominent pulmonary arc produced by the enlarged pulmonary artery as well as the dilated divisions of the pulmonary arteries. The heart is moderately enlarged, with hypertrophy of the left ventricle.

B. In the lateral conventional film the pulmonary vessels are very difficult to recognize because of the complex superimposed shadows.

C. Lateral sectional film of the left pulmonary vessels. The left pulmonary artery (L.P.A.) and vein (L.P.V.) are both greatly enlarged (compare with Figure 3-C). The artery and the vein are separated by the left lower bronchus (L.L.B.). This is the best demonstration of the pulmonary veins that we have been able to get, due probably to the increased size of the vessel.

D. Lateral sectional film of right pulmonary vessels. The film was made at the level of the lung root and gives a cross-sectional view of the dilated trunk of the right pulmonary artery (R.P.A.) and the major branch, which runs downward and only slightly posteriorly. The right pulmonary veins lie medial to this level and consequently are not in view here.

and the oblique views were all made in the recumbent position. The technic is essentially the same as that used in our study of mediastinal tumors and aneurysms by sectional radiography, published last year (10).

With experience we found that usually a single anteroposterior sectional film taken about 1 cm. anterior to the level of the main bronchus gave us an adequate view of the large pulmonary vessels in the horizontal plane. The lateral sectional films were more informative and more useful than the oblique sectional films. The best lateral views of the large pulmonary vessels were obtained on sectional films made

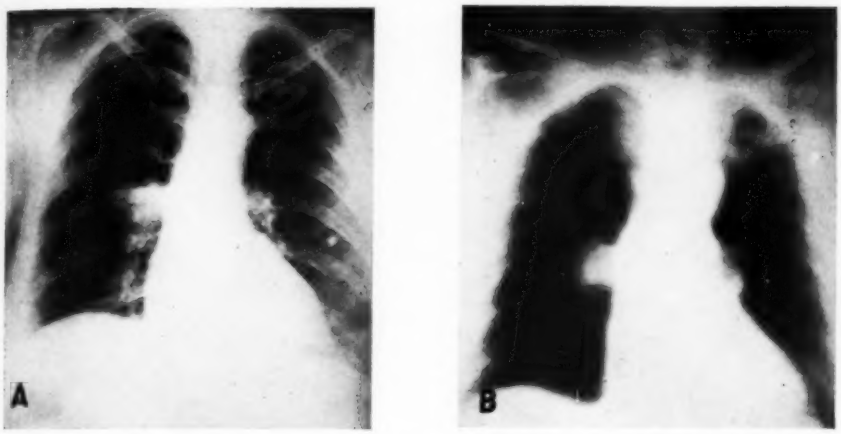

Fig. 6. A and B. Sectional films can be used as an aid in the differentiation of abnormal hilus shadows.

The shadow in the right hilus is in "sharp focus" at a level that is anterior to that of the pulmonary arteries, which are not "in focus." Furthermore, the clear-cut borders of the shadow, together with the absence of branching pulmonary vessels leading from the shadow, distinguish it from the pulmonary artery and identify it as a pulmonary mass.

This patient was a 52-year-old housewife, who for eight months had had a cough, blood-tinged sputum, and pain in the right chest. At a bronchoscopic examination a bronchiogenic carcinoma was found in the right lower bronchus.

across the lung root at approximately the level at which the vessels enter and leave the lung and just medial to the bifurcation of the main bronchus. The distance of the lateral plane from the mid-line necessarily varied between the right and left sides of the chest and also among various individuals. For this reason two or three lateral sectional films had to be made at levels 1.5 cm. apart at the region of the lung root to observe the pulmonary vessels fully.

Figures 3 to 7 represent a series of cases which illustrate the points about the anatomy of the pulmonary vessels that have been discussed. They also demonstrate the advantage of using sectional films in the visualization of the pulmonary vessels.

COMMENT AND CONCLUSIONS

1. Body-section radiography affords a superior method for the visualization of the large pulmonary vessels when compared to conventional radiography. This advantage lies in the fact that sectional radiography blurs out the unwanted shadows and leaves only the structures of interest in clear relief. By this means overlying and obscuring shadows are removed, with resultant increase in contrast of the structures in question.

2. The characteristics of the laminagraph proved eminently satisfactory for this type of work: first, because the complete blurring of the unwanted structures produced by the spiral movement of the roentgen tube and film results in a uniform black background on the sectional films; second, because the exposure time of three to four seconds provides high (200 to 300) milliampere-seconds to supply a maximum of contrast.

3. The film made in the horizontal plane in the anteroposterior position is of value in demonstrating the fan-like spread of the pulmonary arteries into the adjacent lung. In many cases the pulmonary arteries could be distinguished from the pulmonary veins (Fig. 3-A). The right and left pulmonary arteries always lie slightly cephalad to the veins. A film in this position is sometimes of value in the differentiation between small tumors located in the hilus and the large pulmonary vessels (Figs. 6-A and B).

4. Sectional films of the pulmonary vessels made in the lateral sagittal plane

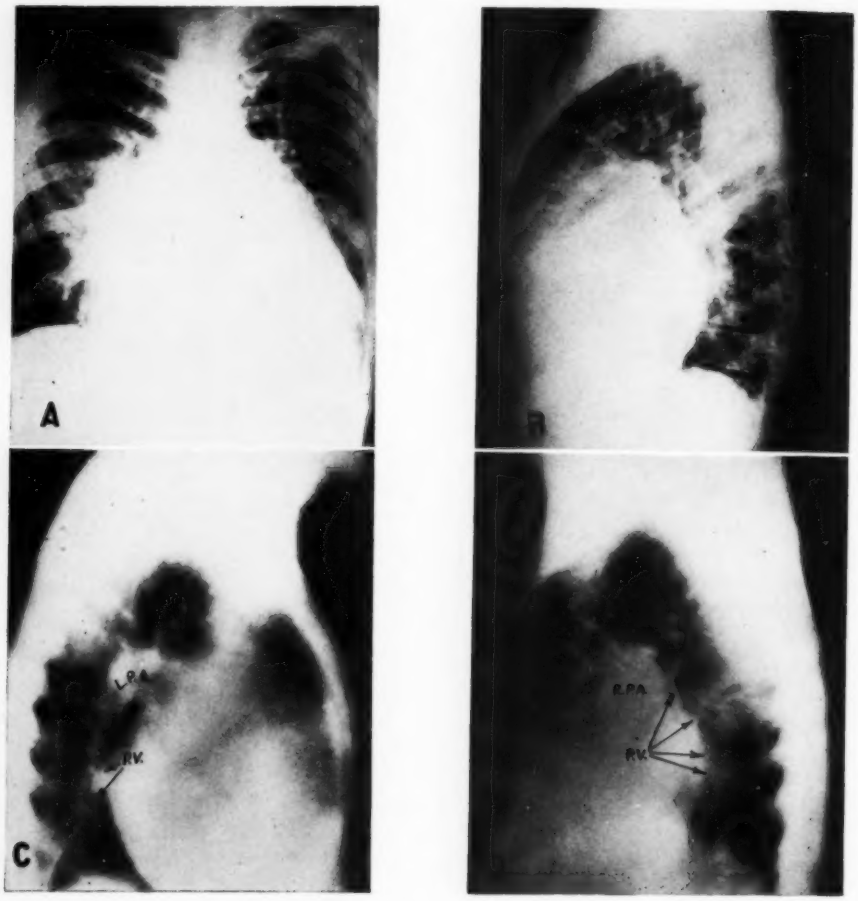

Fig. 7. Pulmonary vessels as seen in rheumatic heart disease with mitral stenosis and insufficiency.

This patient was a 34-year-old man with a history of rheumatic fever in childhood. The physical signs were those of mitral stenosis and insufficiency. For eight months he had complained of intermittent attacks of "rapid heart action," which was the result of fibrillation.

A. Postero-anterior conventional chest film. The heart is greatly enlarged and of the spherical shape that is characteristic of advanced mitral stenosis and insufficiency. The pulmonary vessels are large and congested, but in this film it is difficult to distinguish the pulmonary arteries from the veins.

B. Left lateral conventional chest film. The enlarged left auricle is evident, but here again the pulmonary vessels cannot be accurately identified.

C. Left lateral sectional film. In the left lateral sectional film the left pulmonary artery (L.P.A.) is clearly outlined. It is not enlarged but is of average size. The pulmonary veins (P.V.) form a large mass over the posterior portion of the left auricle. These veins are definitely enlarged. This illustration, as well as Figure 7-D, emphasizes that in mitral stenosis and insufficiency it is the pulmonary veins that are dilated and enlarged rather than the pulmonary arteries.

D. Right lateral sectional film. The trunk of the right pulmonary artery (R.P.A.) is in such intimate contact with the heart that it affords but little contrast in density. The artery is within normal limits. The veins (P.V.) are enlarged and can be seen entering the auricle.

through the lung roots are the best means of visualizing these structures without the use of contrast media. These lateral sectional films offer the great advantage of showing the right and left pulmonary vessels on separate films. The right pulmonary artery and vein are pictured alone on the film, without the superimposed and con-

fusing shadows of the vessels in the opposite lung (Figs. 3-B, C, D; 5-B, C, D). The pulmonary artery and main bronchus are easily recognized in these views, and with them as bearing points the pulmonary veins can be located.

5. In our experience the size and degree of dilatation of the pulmonary vessels, especially the arteries, can be better estimated when observed in the lateral sectional films (see Figs. 3, 4, 5, 7).

6. The detection of dilated pulmonary arteries is important, as this is the only reliable objective sign of disease of the pulmonary arteries. Dilatation of the pulmonary artery is not a characteristic of any one disease but is an indication that any one of many diseases is present, the exact disease to be determined by further clinical and laboratory procedures.

7. The following anatomical facts about the pulmonary vessels can be emphasized from this study. (*a*) The pulmonary vessels exhibit a wide range of variation in the normal size, shape, position, and course. (*b*) The right pulmonary artery is larger in diameter than the left. It ends abruptly at the lung root by dividing into more branches than the left and is therefore more difficult to film. (*c*) The pulmonary veins are harder to visualize than the arteries because they are smaller, have much shorter main trunks, and are consequently in closer contact with the heart.

8. The purpose of Figure 7 is to emphasize that it is primarily the pulmonary veins that are dilated, the pulmonary arteries only slightly so, in patients with mitral stenosis and insufficiency resulting from rheumatic heart disease.

9. Sectional radiography offers another technic for visualizing the main pulmonary vessels. Prior to this method the only other satisfactory means of visualization was by the use of contrast media after the method of Robb and Steinberg.

10. It is the hope of the authors that the advantages gained in the visualization of the large pulmonary vessels will stimulate others, as it has them, to make a conscious effort to observe and study the pulmonary circulation with greater interest and profit.

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DISCUSSION OF SYMPOSIUM ON THE LESSER CIRCULATION

(Papers by Francis L. Chamberlain, Wm. J. Kerr, and Wendell G. Scott and John R. Lionberger)

Earl E. Barth, M.D. (Chicago): It is difficult to know just where to begin the discussion of these excellent papers covering so much material. It appears to me that we might divide the diseases of the lesser circulation etiologically into two main groups—those which involve the cardiovascular system primarily, and a second group which are not primarily cardiovascular but which affect the lesser circulation secondarily. It may be stated that any lesion which will interfere with the circulation of the blood through the lungs, producing an increased pressure within the pulmonary circulation, will result in right-sided cardiac embarrassment. In addition to the etiological factors which have been discussed by Dr. Chamberlain, one might mention the various congenital lesions of the heart and certain nutritional diseases, as well as disturbances in the endocrine system.

One of the criteria necessary for the diagnosis of any disease of the lesser circulation is a demonstra-

tion of enlargement of the right ventricle. This particular phase of the diagnosis is of special interest to us as radiologists. It would seem that the radiologists have been a step behind the internists and cardiologists in the discussion of diseases of lesser circulation in the literature. The anatomy of the pulmonary circulation has been covered by Doctor Chamberlain and Doctor Scott in their excellent papers. Since the right ventricle is placed anteriorly, it is in very close contact with the sternum, and any enlargement which takes place will be either vertical or lateral. An increase in the size of the right ventricle will in most instances result in a rotation of the heart toward the left side, throwing the pulmonary conus into profile. The value of the right anterior oblique position in examining patients suspected of having right-sided cardiac embarrassment should be emphasized. In this position the pulmonary conus can be seen projecting forward, and the posterior border of the heart can be examined in relation to the barium-filled esophagus. By this means any enlargement of the left auricle can be determined.

A word might be said about the anatomy of the right ventricle as compared to the left. Anatomically, the wall of the right ventricle is only about one-third to one-fourth as thick as the left, with the thinnest portion in the region of the pulmonary conus, making it subject to dilatation. As mentioned by Doctor Scott, considerable care must be taken in the interpretation of an enlarged right ventricle merely because there is some prominence in the region of the pulmonary artery or the pulmonary conus. All of us are aware of the fact that in certain long-chested individuals in whom the heart is more or less centrally hung, there may very well be some rotation of the heart toward the left side, thus throwing the pulmonary conus or the pulmonary artery out into profile. In these particular individuals there frequently is a bulge of the cardiovascular shadow in this region. The same finding is often noted in infants and children in whom there is no clinical evidence of cardiac disease.

It would seem, from the work of Doctor Scott on body-section radiography and the work of others on cardiac visualization, that we must change our concept about the structures which produce this bulge in the region of the left hilum. Heretofore I think it has been customary for some of us at least to call this particular shadow the pulmonary conus, but the work of these men would indicate that this is the pulmonary artery rather than the conus. In our own work we have found the kymogram helpful in differentiating tumor masses in the hilar region, particularly when there is marked dilatation of the pulmonary artery and its branches.

I have listened with interest to Dr. Kerr's paper and his very plausible explanation of the cause of precordial pain and right heart embarrassment in certain patients. It should teach us all to stand in the proper position and to avoid obesity.

Doctor Scott has discussed a very valuable addition to our armamentarium in the diagnosis of the diseases of the lesser circulation. I appreciate the opportunity of discussing these interesting and instructive papers.

W. Edward Chamberlain, M. D. (Philadelphia): I should like first to say a word about Doctor Scott's body-section roentgenograms. The difficulty I had in interpreting these, as they were shown, reminds me of my earlier experience with lateral chest roentgenograms, and as in the case of the latter, it will be necessary to take a great many—making the procedure almost a routine—if we are to get the help from them that we need. The primary task of roentgenography, as I see it, is to visualize for ourselves and the referring physician the gross anatomy and pathology, and these I believe are demonstrated by body-section roentgenography better than in any other way. I had an interesting example of this when a physician, with no roentgen experience, made an accurate diagnosis from one of my body-section roentgenograms of the mediastinum, solely on the basis of his pathologic experience.

Dr. Kerr's work is extremely interesting and stimulating. I can demonstrate in a model of the cardiovascular system which I have some of the very things which he has discussed. Thus I can bring about a rise in blood pressure by seeing that the auricle receives a better charge and therefore a more efficient output.

Dr. Chamberlain's presentation is concerned with fundamentals Pulmonary fibrosis and the interstitial type of pulmonary metastases give the same x-ray picture and this is to be expected. In the one case we have merely an increase of fibrous tissue and in the other the plastic reaction that accompanies a neoplastic process. When the roentgenologist hears the words pulmonary metastases he is likely to think of circumscribed deposits—"cannon-ball" metastases—but I feel sure that Dr. Chamberlain had reference to that type of metastatic growth that is interstitial in its distribution.

Acquired Subtentorial Pressure Diverticulum of a Cerebral Lateral Ventricle[1]

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New York, N. Y.

ACQUIRED subtentorial pressure diverticulum of a lateral ventricle is a condition in which a part of the medial portion of the atrium of a lateral ventricle extends medially and caudally through the tentorial incisure to exist as an accessory infratentorial fluid-filled sac. It is important that this lesion be generally recognized, for it may be confused with an enlarged and rostrally displaced fourth ventricle, which would lead to an incorrect diagnosis and wrong therapeutic measures.

Localized defects in the brain are usually congenital, traumatic, or vascular in origin. They may also follow an osteoplastic flap or subtemporal decompression in the presence of a subtentorial obstruction to the egress of cerebrospinal fluid. In such cases the homolateral temporal horn enlarges and may herniate through the defect in the skull and form a large cavity beneath the temporal muscle.

LITERATURE

There are no reports in the literature of the condition described in this communication, although there are numerous reports of cerebral defects due to other causes. Thus Cruveilhier in his *Anatomie pathologique* (1829–35) described and depicted by drawings the brains of several idiots that were congenitally defective. In one there was a defect in the left temporal lobe by which the lateral ventricle communicated with the subarachnoid space. Heschl, in 1859, described three patients of his own who had defects in the brain and he briefly reviewed and recorded two cases reported by Rokitansky (1853), one by Deschamps (1833), and one by Romberg (1842). Heschl described defects in the brain as of four types: (1) a meshwork cavity in the brain filled with serous fluid, not connecting with either the ventricle or the subarachnoid space; (2) such a cavity communicating with the ventricle and not with the subarachnoid space; (3) such a cavity connecting with both the ventricle and the subarachnoid space; (4) a possible fourth such cavity connecting only with the subarachnoid space, though Heschl had no example of this type of defect and it was therefore necessary for him to theorize on this lesion.

CASE REPORTS

The material which forms the basis of this presentation consists of three cases, one of which was verified at necropsy; the diagnosis was made in two instances from the pneumencephalograms.[2]

CASE I (patient of Drs. Peterson and Baker[3]): *Spells of unconsciousness of five months' duration. Plain roentgenograms of skull revealed changes indicating markedly increased intracranial pressure. Ventriculography disclosed an advanced degree of internal hydrocephalus and an unusual collection of gas beneath the tentorium. Left parietal exploration showed a cyst-like area occupying the superior portion of the vermis. Patient expired. At necropsy, a diverticulum of the left lateral ventricle was disclosed.*

H. O., male, aged 29 years, was admitted to the University of Minnesota Hospital during the latter part of December 1938. He had been subject for five months to spells of unconsciousness, and during a recent attack had fallen down fifteen steps.

On examination the patient was not co-operative and showed marked memory impairment for both recent and remote events. A Babinski toe sign was

[1] From the Department of Radiology, College of Physicians and Surgeons, Columbia University, and the Neurological Institute, New York City. Presented in part as the Presidential Address before the Harvey Cushing Society, Rochester, N. Y., May 30, 1941. Accepted for publication in April 1942.

[2] I am indebted to Drs. Harold O. Peterson and A. B. Baker, radiologist and pathologist, respectively, of the University of Minnesota, for the use of Case I, and to Dr. William German of New Haven for Case III.

[3] This case of Drs. Peterson and Baker has been reported and discussed from another point of view (Case 6) in Am. J. of Roentgenol. **46**: 44, July 1941.

elicited bilaterally and unsustained ankle clonus was present on the right. There was no papilledema. The spinal fluid pressure was 16 to 18 mm. of mercury.

Encephalography was performed and a small amount of air entered the lateral ventricles, showing them to be markedly enlarged. The rest of the ventricular system was not visualized.

Ventriculography was done on Jan. 6, 1939, and the ventriculograms showed the lateral and third ventricles to be greatly enlarged. The aqueduct of Sylvius was not visualized. Beneath the tentorium was a large collection of gas, which was believed to be in a cyst in the cerebellum connecting with the ventricular system (Fig. 1). Ventriculography was immediately followed by a left posterior parietal craniotomy. The tentorium was split and a cystic cavity was seen superior and anterior to the cerebellum, displacing the latter backwards. The cyst was incised and measured about 2.5 *inches* in diameter. It contained no tumor and was believed to represent a porencephaly. The patient became increasingly comatose and died on Jan. 14, 1939, eight days after operation.

At necropsy the lateral and third ventricles and the rostral portion of the aqueduct of Sylvius were markedly enlarged. The posterior horn of the left lateral ventricle extended medially and posteriorly through the tentorial notch to occupy a position along the superior border of the cerebellum. The aqueduct was completely occluded in its mid portion by a diffuse astrocytoma of the mesencephalon.

Comment: Case I, to recapitulate, was that of a young man who had had attacks of unconsciousness for five months prior to admission to the hospital. The plain skull films showed evidence of prolonged and advanced increased intracranial pressure. The pneumencephalograms showed marked enlargement of the lateral and third ventricles and an unusually large collection of gas beneath the tentorium, which at necropsy proved to be a diverticulum of the left lateral ventricle.

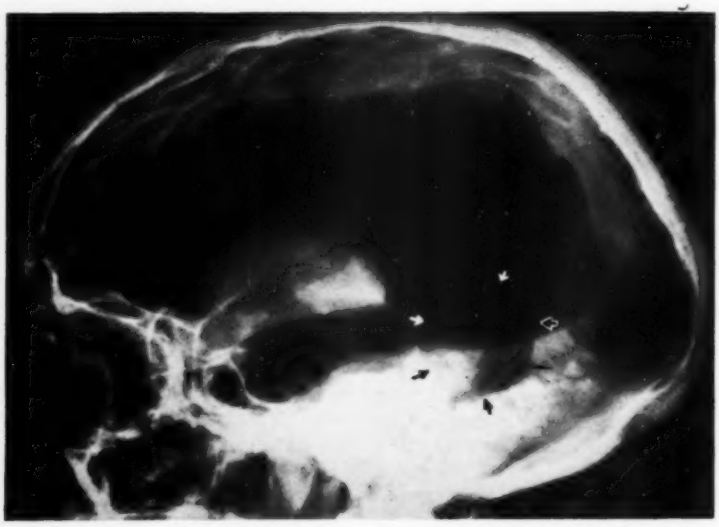

Fig. 1. Case I: Astrocytoma of mid brain with aqueduct stenosis. Lateral pneumencephalogram showing the large diverticulum (2) outlined by arrows. Courtesy of Drs. Leo Rigler, Harold Peterson, and A. B. Baker.

CASE II (author's patient): *Paresthesias of the left side of the face and body associated with sudden temporary paralysis of the left extremities. Homolateral muscular atrophy, severe headache, diminished visual acuity, incontinence, nausea and vomiting. Recently left hemiparesis. Early papilledema. Ventriculograms revealed markedly depressed bodies of the lateral ventricles and third ventricle, large collection of gas in the position of the vermis of the cerebellum, deformed fourth ventricle. Removal of parasagittal meningioma. Recovery.*

A. S., a single 46-year-old domestic, was admitted to the Neurological Institute of New York on Feb. 12, 1941. Since 1936 she had experienced a sensation of pins and needles in the left side of the face and body. This was associated with sudden loss of power in the extremities on the left side, and was followed by wasting of the muscles. Suddenly one night she

had an attack in which the left side of the body was affected with a sensation of being stuck with pins and needles. Somewhat later she developed severe headache localized to the right vertex and parieto-occipital areas. The headaches were accompanied by a gradual loss of visual acuity, incontinence, nausea, and vomiting. Recently, the left-sided paresis had become so great that the patient was no longer able to get about, and several weeks prior to her admission she tripped and fell down a flight of stairs. Following this accident, her headache increased and was accompanied by severe nausea and vomiting. During the last few years, there had been a loss of over 50 pounds in weight.

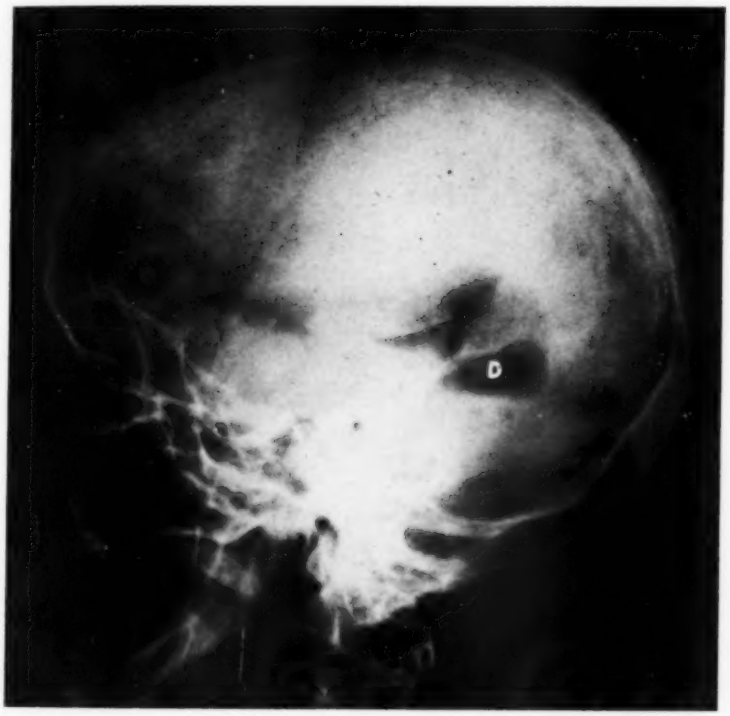

Fig. 2. Case II: Right parasagittal meningioma. Lateral pneumencephalogram showing the marked ventral displacement of the bodies of the lateral ventricles, and the diverticulum (D).

The patient was admitted to the Mary Imogene Bassett Hospital, Cooperstown, N. Y., on Feb. 12, 1941, and for the first time in four admissions since 1936 it was noted that she had early papilledema. Because of this she was transferred to the Neurological Institute for further investigation and treatment.

The family and personal histories were negative.

On examination the patient was semicomatose and had a strong odor of acetone on her breath. She was incontinent, bedridden, and had a left hemiparesis. There were tenderness over the right side of the head, particularly in the parieto-occipital region, and a paresis of the left side of the face. The blood pressure was 140/85. The gait could not be tested and there was generalized atrophy and weakness of the muscles on the left. The non-equilibratory tests on the right side were performed quite well, but could not be performed on the left. All skilled acts, including writing, were poorly done. Speech was slow, hesitant, and slurred, and the test phrases could not be repeated. The reflexes were hyperactive bilaterally, but somewhat more so on the left, where there was a Babinski toe sign. The sensory examination disclosed a loss of about 20 per cent, with hyperpathia or dysesthesia in the left leg and side of body. There was a marked loss of the muscle tendon sense in the left foot and arm. Stereognosis was normal in the right hand and impaired in the left. The sense of smell was intact, but there was bilateral impairment of visual acuity, which was more marked on the left side. The visual fields could not be tested due to the patient's inability to co-operate. The right pupil was larger than the left, while the right palpebral fissure was smaller than the opposite one. There was bilateral papilledema of

Fig. 3. Case II: Sagittal laminagram showing the atrium (A) of one of the lateral ventricles, diverticulum (D), indicated by arrows, and fourth ventricle (V) markedly compressed and displaced ventrally.

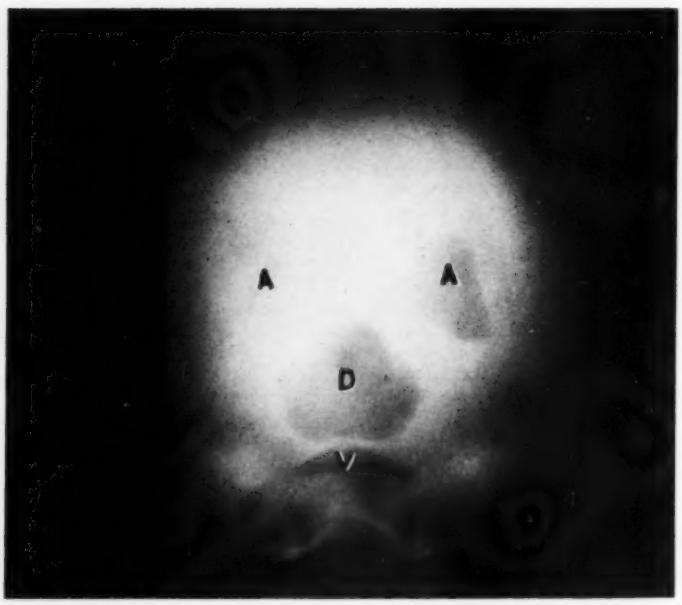

Fig. 4. Case II: Coronal section of pneumencephalogram through the atria (A) of the lateral ventricles, diverticulum (D) and fourth ventricle (V).

four diopters. The cranial nerves, except for the optic nerve, were intact. The patient co-operated poorly and she was of a low mental level.

Examination of the blood revealed a hemoglobin of 50, a red cell count of 2,340,000, and 5,500 white cells, with a normal differential count. The blood chemistry showed nothing of significance, and the Kline test was negative. The urine analysis revealed albumin 1+, acetone 2+, and a trace of glucose.

The electro-encephalogram was markedly abnormal, with medium- to high-voltage waves (one to three per second) on both sides, but this was more evident on the right.

of gas, which represented the much compressed fourth ventricle (Figs. 3 and 4).

The patient was operated upon on Feb. 18, 1941, when a large right parasagittal meningioma was removed. She made a satisfactory recovery and was discharged from the hospital on March 16, 1941. She was readmitted to the Neurological Institute on June 16, 1941, and encephalograms on June 25 showed the diverticulum to be still present, though it had definitely decreased in size since the first examination. The lateral ventricles were considerably larger than in the initial pneumencephalograms. The cerebral and cerebellar structures, however,

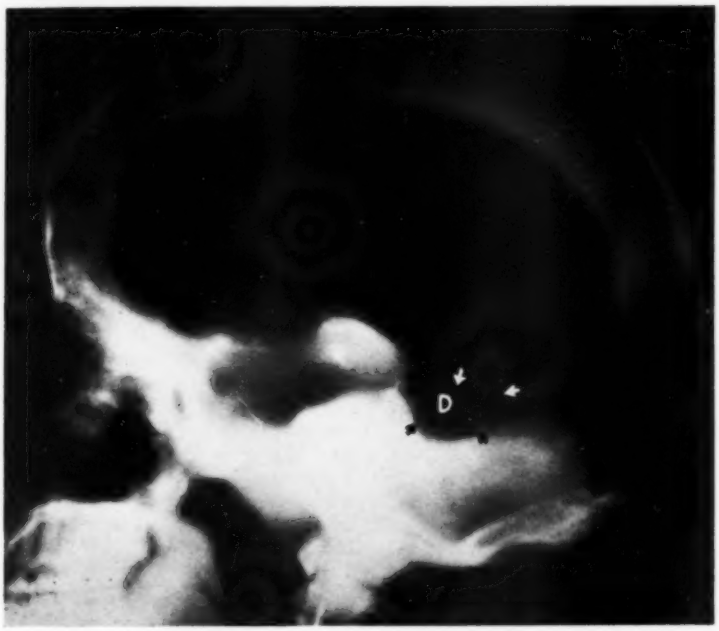

Fig. 5. Case III: Aqueduct stenosis. Sagittal laminagram showing marked enlargement of the lateral and third ventricles, and the moderate sized diverticulum (D), indicated by arrows. Courtesy of Dr. William German.

The roentgen examination disclosed atrophy of the floor, posterior clinoid processes, and dorsum sellae, but no other abnormal findings. This led to a diagnosis of an unlocalizable intracranial tumor.

Ventriculography on Feb. 18, 1941, showed the lateral and third ventricles to be within normal limits in size. The bodies of the lateral ventricles were displaced ventrally to a marked degree (Fig. 2). The third ventricle was similarly displaced and the prepineal portion was moved caudally. Beneath the tentorium cerebelli was a large collection of gas, which measured on the roentgenogram 4.5 × 4.5 × 3.5 cm. This occupied the usual position of the superior portion of the vermis of the cerebellum. Directly beneath it was a narrow slit-like collection occupied a more normal position. The bone flap was found to be infected and the involved portion was removed on July 1, 1941. The patient made an uneventful recovery from the operation and at the time of discharge the drainage from the wound had ceased. She was last heard from on Dec. 2, 1941, at which time she reported she had returned to work as a domestic.

Comment: In the case reported above a parasagittal meningioma had produced marked deformity of the brain. The ventriculograms showed an abnormal gas-filled cavity beneath the tentorium, which

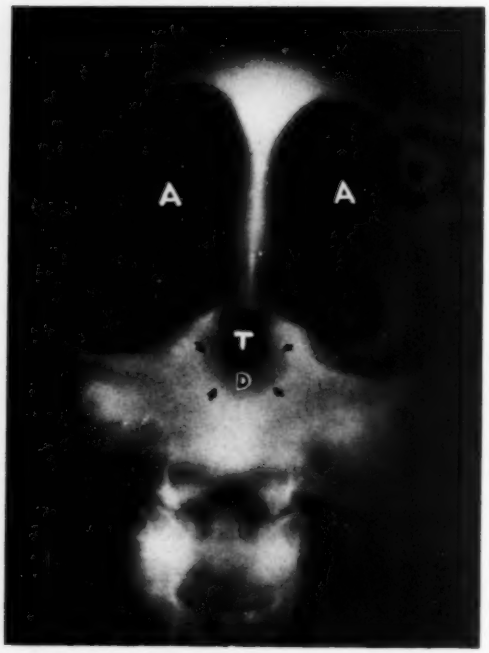

Fig. 6. Case III: Coronal laminagram showing the dilated lateral ventricles (A), third ventricle (T), and diverticulum (D).

undoubtedly represented a pressure diverticulum of a lateral ventricle.

CASE III (patient of Dr. William German): *Diplopia, amenorrhea, loss of "pep," and headache. Papilledema. Ventriculography. Operation: resection of scar in aqueduct of Sylvius. Recovery.*

R. G., a girl of 16 years, was admitted to the New Haven Hospital on July 9, 1940. She gave a history of transient diplopia five years earlier, the onset coinciding with a severe attack of measles, and of amenorrhea for three years. For approximately eighteen months she had experienced progressive loss of energy and for the last six months severe occipital headaches. She had no nausea, vomiting, weakness, convulsions, or fainting spells. Three years before admission the patient had a severe attack of scarlet fever, after which she had a period lasting two days, followed by complete amenorrhea.

No localizing symptoms were present. The family history was non-contributory. The past history was not of essential significance. A tonsillectomy had been performed at the age of four years. The patient at the present time was attending high school.

Physical examination revealed a well developed and well nourished white female, quite tall. There was no deformity or tenderness of the skull. Ears and throat were negative. The chest was clear to percussion and auscultation. There was no tenderness in the abdomen. The extremities, aside from being slightly obese, were physiologically normal. Neurological examination showed cerebration generally intact; cranial nerves generally intact, save for optic nerve, which showed papilledema, 1 1/2 diopters on right, 2 diopters on left; bilateral lower nasal quadrant visual field defect. The motor and sensory systems seemed to be intact throughout the remainder of the body. Reflexes were slightly hyperactive but symmetrical.

Following admission the patient was seen by Dr. James Fox, who suspected an intracranial tumor and advised ventriculography. A glucose tolerance test done shortly after admission showed marked hypertolerance. Seven days after admission, a ventriculogram was made, which showed greatly dilated lateral ventricles (Figs. 5 and 6). Following this, a Torkildsen procedure was done on July 17, connecting the posterior horn of the right lateral ventricle to the cisterna magna by means of a catheter. On July 23 a combined ventricular and lumbar puncture was done, showing increased pressure in the ventricles, indicating a stenosis of the aqueduct of Sylvius. A cerebellar craniotomy was done on Aug. 22, with division of a stenotic band at the lower end of the aqueduct of Sylvius. The catheter previously placed in the lateral ventricle connecting it to the cisterna magna was then removed. A diagnosis of stenosed aqueduct of Sylvius was made. The cerebellar vermis was transected until the lower end of the aqueduct of Sylvius was exposed. A dense scar occluding the aqueduct was removed from its roof; a catheter then passed freely into the third ventricle. The scar was composed of astroglial elements with no evidence of inflammatory cells. Frequent ventricular punctures were required, followed first by combined ventricular and lumbar puncture and later lumbar puncture alone, over a period of two months. Recovery was quite slow, and walking was most difficult until the middle of November 1940. The patient was discharged from the hospital Nov. 21, 1940, at which time she still required assistance while walking. There was a convergent squint, and vomiting occurred frequently on change of position. The suboccipital decompression was soft and the papilledema had completely disappeared.

DISCUSSION

The title, "Acquired Subtentorial Pressure Diverticulum of a Cerebral Lateral Ventricle," has been used to indicate the nature of the process described here and to differentiate it from other forms of cerebral defect.

The cases presented in this paper are of interest in several respects. Of greatest importance is the matter of diagnosis, for in shape the diverticulum often is not un-

like a greatly dilated fourth ventricle and may be confused with the latter. The diverticulum, however, usually occupies a position too high for the fourth ventricle and in most cases it is much larger, except when the latter is enlarged as a result of an obstruction to the foramina for the egress of the cerebrospinal fluid from this cavity. In the first case the markedly enlarged lateral and third ventricles might very well have led to an interpretation of the diverticulum as an enlarged fourth ventricle, and to a diagnosis of tumor or arachnoiditis in the posterior fossa. In the second case, where a supratentorial, parasagittal tumor was obviously present, the diverticulum could not have been mistaken for an enlarged fourth ventricle due to a caudally placed cerebellar tumor, unless a multiple tumor diagnosis were made.

The site of the defect in the brain is also of great interest. In the present series of cases the portion of the medial wall of the lateral ventricle that gave way and permitted the diverticulum to form was apparently the hippocampal gyrus. Unfortunately, the brain specimen of the first case is no longer available for study, but according to Dr. Baker's report the site of the out-pouching of the ventricle probably was the posterior portion of the hippocampal gyrus. In the second case the study of the ventriculograms stereoscopically showed the diverticulum apparently arising from the atrium of the right lateral ventricle.

The distance that the medial wall of the ventricle must migrate to reach the edge of the tentorium is negligible, for normally the medial margin of the atrium and the posterior third of the body of the lateral ventricle are practically in the same vertical plane as the free edge of the tentorium. Furthermore, this obtains at the exact area where the hippocampus swings laterally from the thalamus, and the gyrus between the forceps major and splenium is quite thin. Therefore, when the lateral ventricles are enlarged, particularly when they are markedly dilated, the medial portion of the atrium of the lateral ventricle probably is actually medial to the free edge of the tentorium, thereby facilitating the formation of a subtentorial diverticulum.

The underlying cause for the subtentorial position of the diverticulum in all three instances was marked elevation of the intracranial pressure, and especially the intraventricular pressure. It would seem that the local elevation of pressure in the atrium, which led to the formation of the diverticulum, can be explained more readily in the first and third cases with enlargement of the lateral and third ventricles, for in these the fluid was obstructed at the mid point of the aqueduct of Sylvius. The pressure distal to this point was therefore less than proximal. Furthermore, part of the atrial portion and the posterior third of the body of the lateral ventricle lie distal to the obstruction, with the result that this portion of the ventricle would be supported less on its medial margin than the part rostral to the site of the obstruction, thereby permitting out-pouching of the ventricle to occur and also allowing the latter to migrate caudally.

The patient with the parasagittal meningioma had normal-sized but markedly deformed lateral and third ventricles, with ventral displacement of the body and splenium of the corpus callosum, thalami, and fornices. In the mid-sagittal laminagrams it was evident that the above had taken place and, in addition, that there had been a caudal migration of these structures as well. The tumor was a large one, and in the displacement of the brain structures enumerated above, the atrium and adjacent portion of the right lateral ventricle were carried along through the tentorial notch. The formation of the diverticulum was probably facilitated by an obliteration of the anterior portion of the body of the right lateral ventricle so that the cerebrospinal fluid forming in the atrial and temporal portions of the homolateral cavity could not escape by way of the interventricular foramen, but caused a localized elevation of the intraventricular fluid pressure.

In Case III the stenosis of the aqueduct

caused a marked elevation of intracranial pressure and the mechanism for the production of the obstruction was similar to that in Case I.

The nature of the wall of the diverticulum cannot at present be determined except that it probably consists of a thin layer of brain tissue and leptomeninges, and may very well be ependymal-lined.

SUMMARY AND CONCLUSIONS

1. Three cases showing a large subtentorial fluid-filled cavity have been presented.

2. The site of the cerebral defect, the mode of its production, and the importance of its recognition have been discussed.

3. It is proposed that this condition be called "acquired subtentorial pressure diverticulum of a cerebral lateral ventricle."

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Tumors of the Urinary Bladder[1]

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SYMPTOMS OF bladder tumors and of prostatic obstruction were probably recognized by Hippocrates, and later by Galen. According to Beer (5), the first important contribution to the subject was Lacuna's monograph, in 1551, on methods of recognition and removal of caruncles of the neck of the bladder. In 1639 Covillard did the first recorded surgical operation for tumor of the bladder. The first attempt to remove the upper two-thirds of the bladder with its peritoneal covering is attributed to Sonnenburg, some years later. Until the time of Billroth, however, no great progress in this field was made. In 1874 he first successfully removed a bladder tumor under visual control, through a suprapubic approach. Beer (5) credits Bardenheuer, in 1887, with the first successful total cystectomy. Hinman and Smith (22), however, state that Bardenheuer's patient died; they attribute the first successful total cystectomy to Pawlik.

In 1877, Max Nitze, in Dresden, devised the first satisfactory cystoscope. In 1886, the electric bulb replaced the hot platinum wire for visualization, and subsequent development of the cystoscope was rapid, being paralleled by a steady improvement in the treatment of bladder tumors, especially benign papillomas. Nitze successfully removed many benign growths cystoscopically by means of a heated wire loop soon after 1900 (3). In 1910 Beer (3, 5) introduced fulguration of papilloma of the bladder. Various operative technics have been devised, but are outside the scope of this paper.

Cleves of Philadelphia first used radium in the bladder (3) in 1903. In 1919 Duane and Barringer (3) employed glass radon seeds in carcinoma of the bladder, and in 1924 the glass was replaced by gold. X-rays have been used in the treatment of vesical tumors for many years, both in conjunction with other forms of treatment and, in some cases, alone. They have been utilized for external irradiation and contact therapy (15, 19, 20, 23). Recently supervoltage therapy has been employed (10, 16). Our method is described later in these pages.

This paper is a report of 174 cases of tumor of the bladder treated at the University Hospitals, University of Minnesota Medical School, from Jan. 1, 1930, through Dec. 31, 1939. These cases have been divided into three groups: (1) benign papilloma, (2) papillary carcinoma, (3) infiltrating carcinoma. This classification is used because of its simplicity, though the merits of other classifications, as those of Broders and the Bladder Tumor Registry of the American Urological Association, are acknowledged.

There were in this series 28 benign papillomas and 146 carcinomas, 57 of which were papillary (39 per cent) and 89 infiltrating (61 per cent). Most of the carcinomas were too extensive to permit of radical operation. Barringer (4) reported 39.4 per cent papillary and 60.6 per cent infiltrating carcinomas in his group, and Ferguson (18) 45 per cent papillary and 55 per cent infiltrating. Watson and Herger (27), on the other hand, found about 60 per cent in a series of 445 cases to be of the papillary type.

There were 142 males and 32 females in our series, a ratio of about 4.5 to 1. Beer (5) gives the usual ratio as 4 to 1. The average age in the benign group was 62.3 years, the youngest patient being twenty-five and the oldest seventy-seven. In the malignant group, the youngest patient was thirty-seven and the oldest eighty-five

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(average 63.1). Of the 146 carcinomas, 93 occurred between the ages of fifty and seventy (63.7 per cent). Of the papillomas, 19 were in the fifty- to seventy-year group (67.8 per cent). Bumpus and Silver (7) gave 57.5 years as the average age in their series, and stated that 56 per cent of their patients were in or above the seventh decade. Butler (9) quotes the Carcinoma Registry as stating that 62 per cent of bladder carcinomas occur in the fifth and sixth decades. Ash (1), in a report of the Bladder Tumor Registry, states that 80 per cent occur after fifty years of age. The youngest patient in the Carcinoma Registry was a male seventeen years of age. Carcinoma of the bladder is rare before the fourth decade.

Among the papillomas there were 4 multiple and 24 solitary tumors. Sixteen of the carcinomas were multiple and 130 solitary. Barringer (2) reported 58 multiple and 159 solitary cases in his series. Recurrences are not considered as multiple tumors.

The frequency of metastasis varies considerably in different reported series. Burkland and Leadbetter (8) quote Cunningham as finding metastases reported in 32.3 per cent of a large series from the literature. Spooner found metastases in 29 per cent of a series at the Mayo Clinic. Ash (1) reported 288 cases with metastases in a group of 1668 (17.2 per cent). Of our patients 35 (24 per cent) had demonstrable metastatic lesions. These figures indicate that metastasis in carcinoma of the bladder is so frequent as to require a careful search before any radical surgical procedure is considered. Burkland and Leadbetter (8) stress the importance of obtaining roentgenograms of the lungs and bones, especially the bones of the pelvis.

SYMPTOMS

In the cases of papilloma, the shortest duration of symptoms was three days and the longest fourteen years (average 2.6 years). In the carcinoma cases, the shortest history was two weeks, and the longest twenty years (average 2.3 years). While it may well be questioned whether symptoms of twenty years' standing were due throughout that period to carcinoma, the important fact is that in the average case symptoms were present for one or two years before a diagnosis was made. This point is stressed by many writers.

Hematuria was the first symptom in 150 cases (85 per cent). This agrees well with statements in the literature (5, 9, 18). More often than not, the hematuria is intermittent and painless. Even though it be of apparently insignificant duration and severity, however, it demands a thorough search for tumor of the bladder or kidney. Unless the hematuria can be adequately explained otherwise (and it rarely can be), the patient is entitled at least to excretory urography and cystoscopic examination by a competent urologist. Cystography may be done if deemed advisable (9, 18). It would seem that the public has not been sufficiently educated as to the significance of hematuria.

Increased frequency and dysuria were the next most common symptoms, being present in approximately one-third of the cases. Nocturia was present in about 15 per cent. Other symptoms, occasionally noted, were incontinence, a sense of incomplete emptying of the bladder, pain over the region of the bladder, and renal colic.

RESULTS OF TREATMENT IN PAPILLOMA

The treatment administered in the 28 cases of papilloma was as follows: fulguration plus radon in 4; excision plus x-ray irradiation in 1; fulguration plus x-ray in 1; resection only in 2; fulguration only in 19. In 1 case no treatment was given. Nine patients had recurrences. The results of treatment are given in Table I. It will be noted that of the 14 patients treated up to and including 1935, 11 are alive after five years.

Fulguration or removal by cutting current is undoubtedly the treatment of choice for benign papillomas. There is often a question, however, whether or not the lesion is benign; in such cases other forms of treatment, as radon implantation

TABLE I: PAPILLOMA OF THE BLADDER (28 CASES): RESULTS OF TREATMENT

Date	No. of cases	Years Survival									
		1	2	3	4	5	6	7	8	9	10
1930	2	1	1	1	1	1	1	1	1	1	1
1931	0	0	0	0	0	0	0	0	0	0	
1932	1	1	1	1	1	1	1	1	1		
1933	2	2	2	2	2	2	0	0			
1934	6	6	6	6	6	6	4				
1935	3	2	2	2	1	1					
1936	3	3	3	3	1						
1937	3	3	3	2							
1938	7	6	4								
1939	1	1									

or external radiation, are added. Beer (5) reported 248 cases, all but 25 of which were treated by fulguration. Of 160 of his patients who were followed from one to twenty-four years, 62 showed recurrences at some time. Recurrence was observed as late as nineteen years after the first treatment.

TREATMENT OF CARCINOMA

While the treatment of benign papilloma has been well established and the results are reasonably satisfactory, carcinoma of the bladder presents an entirely different problem. The various forms of treatment may be summarized as follows (5, 19):

1. Surgical removal.
   (*a*) Destruction by diathermy or cautery (transurethral or suprapubic).
   (*b*) Excision of the tumor with part of the bladder.
   (*c*) Total cystectomy.
2. Implantation of radium needles or radon seeds.
3. X-ray therapy.
   (*a*) External irradiation.
   (*b*) Contact therapy.
4. Various combinations of the above.

Each of the procedures listed above has its indications and contraindications, and there is considerable difference of opinion as to the efficacy of each.

Fulguration with Current or a Surgical Diathermy Apparatus: In 1935, Counseller and Braasch (12) reported astonishingly good results from suprapubic diathermy alone. They state: "Seventeen patients whose condition was considered inoperable were treated extensively with diathermy only, and 15 of the 17, or 88 per cent, lived more than five years." The others died from unrelated conditions. Bumpus and Silver (7) used diathermy in 77 patients and in 25 obtained "apparent cures" of three to five years' duration. They write: "No other form of treatment of tumors of the bladder proved as efficacious." So far as we are able to ascertain, the results of Counseller and Braasch have never been attained, or even approached, by other investigators, with fulguration or any other form of treatment, and it is probable that their report deals with a selected group. There is no doubt that some tumors can be satisfactorily eradicated by this method.

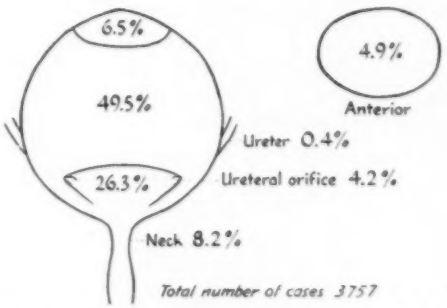

Fig. 1. Distribution of bladder tumors, modified from Ash (1).

Fulguration is also a valuable adjunct to other forms of treatment. If a considerable part of the tumor can be removed, radon and x-rays, especially in the form of contact therapy, can be utilized to much greater advantage. Pfahler and Sampson (25) report a case in which 6,500 r were delivered to the tumor by external irradiation in 1933. Four months later the tumor, which was originally 6 cm. in diameter, was reduced to only 10 per cent of its former size. This residue was destroyed by electrocoagulation through the cystoscope, and in 1941 the patient was entirely free from signs and symptoms. Watson and Herger (27) also report the satisfactory use of electrocoagulation after external x-ray therapy.

Partial Resection: If the tumor is so situated that it can be adequately removed without disturbing the function of the

bladder to a great extent, resection would seem to be the treatment of choice. Unfortunately, however, the vast majority of tumors are not so situated. Ash (1) gives some interesting data relative to the location of bladder tumors as determined by the Carcinoma Registry in over 2,700 cases. Over two-thirds are located in the physiologically indispensable part of the bladder, the posterior wall including the trigone and neck (Fig. 1). Ferguson (18) reports that 50 per cent of his series occurred in the lateral walls and 26 per cent in the neck and trigone. It seems obvious, therefore, that a relatively small percentage of tumors can be considered eligible for this form of treatment, unless they are small, which means early.

Total Cystectomy: In the presence of extensive lesions or of lesions involving vital parts of the bladder, and therefore excluding the possibility of partial resection, total cystectomy has frequently been undertaken. This procedure has some ardent proponents and also many opponents. Beer (5, 6) concludes that resection of the tumor or total cystectomy when necessary, rather than electrocoagulation or radium therapy, is the method of choice, especially in the infiltrating types. Orr, Carson, and Novak (24) report interesting results from total cystectomy as determined by questionnaires addressed to numerous clinics and surgeons.

18	surgeons reported	29	cases,	mortality	100%
16	" "	67	"	"	50–100%
13	" "	106	"	"	25–50%
21	" "	151	"	"	0–25%

Average mortality 33.2%

The above figures do not include the operative deaths due to the preliminary ureteral transplantations. If these are added, the average is greatly increased. Only 18 patients survived five years (5 per cent). The authors quote the Carcinoma Registry as showing the average five-year survival rate as being 23 per cent, with 15.9 per cent with no evidence of disease after five years. It does not seem, therefore, that total cystectomy will increase the five-year survival rate in bladder tumors. Of the 267 surgeons reporting, only 8 favored radical treatment. Goin and Hoffman (19) estimate the primary mortality of total cystectomy at 50 per cent.

Use of Radium Needles or Radon: There is a great difference of opinion as to the value of radium or radon in carcinoma of the bladder. Beer (5) considers partial resection and total cystectomy as far superior. The implantation of radon, he declares, is always a hit-and-miss affair, since "one cannot accurately delimit the extent of the infiltrative process by sight or by palpation from within the bladder." He quotes the Carcinoma Registry as stating that radon gives 8.8 per cent five-year cures and partial cystectomy 18.5 per cent (6). Ferguson (18) also discourages the use of radium, because of ulceration and increase in infection. Barringer (3), on the other hand, favors radon therapy. In a rather extensive article, in 1940 (4), he reports 228 consecutive cases, of which 214 were treated with radium. In this latter group there were 71, or 33.1 per cent, five-year survivals. Twenty-six of the 214 were cured of the carcinoma but died of other causes. Eliminating these 26 cases, he obtains a five-year survival of 37.8 per cent. Dean (13) states that a combination of external and interstitial radiation should give better results than either one alone; he stresses the fact that 12 threshold erythema doses is the average amount of radiation necessary for the successful treatment of bladder carcinoma. It is possible that at least part of the failure of both x-ray and radium has been due to insufficient dosage. Dean and Balfour (14) state that they give up to 75 or 80 millicuries of radon, using 2 millicurie gold seeds. They have had no deaths from the local destructive action of the gold seeds. Harris (21) says that up to 50 radon seeds of 2 millicuries each may be safely used by experts. Whether or not these large doses are given in one sitting is not stated.

X-ray Therapy: Earlier reports on roentgen therapy of bladder tumors were

TABLE II: CARCINOMA OF BLADDER: SURVIVALS AFTER FIRST TREATMENT

Years	No. of cases	Years Survival									
		1	2	3	4	5	6	7	8	9	10
1930	6	2	2	1	1	1	0	0	0	0	0
1931	7	5	4	3	3	3	2	1	0	0	
1932	9	4	1	0	0	0	0	0	0		
1933	11	4	4	4	3	1	1	0			
1934	14	5	3	3	3	1	0				
1935	23	11	9	9	8	3					
1936	23	11	10	8	8						
1937	19	6	4	2							
1938	19	9	6								
1939	15	4									

enthusiastic, but as the cases were followed, the results were less gratifying. Five-year survivals are rare, but symptomatic relief is sometimes obtained.

With the more recent forms of irradiation, especially supervoltage and contact therapy, a new and better avenue of approach may have been found. Beer (5) did not consider external x-ray therapy of any appreciable value. Ferguson (18) does not believe that it will wholly destroy the tumor but does believe that the size of the growth may be decreased and symptoms relieved. Rather recently, contact therapy, usually with the Chaoul tube, has been tried (15, 19, 20, 23). Goin and Hoffman (19) now use a suprapubic cystotomy rather than the marsupialization which they formerly employed to permit contact treatment. The elapsed time since treatment (one to nineteen months) in their series is too short for determination of final results. Supervoltage x-rays have been used for some time, but here again the interval is too brief for definite conclusions. Dresser and Rude (16) have gained the impression that the results from million-volt equipment are better than those obtained with the lower voltages. Schumacher and Steel (26) reported 15 cases, with 9 patients alive (2 more than one year) at the time of writing. Colby (10, 11), using a million-volt unit, found that infiltrating tumors responded better than papillary growths, but he reported only 24 cases. He concluded that the dosage was still unsettled but that, since a regression occurred in a majority of cases, the method deserved further trial.

Cases at the University Hospital receiving x-ray therapy either alone or as a supplement to other forms of treatment have been divided into four groups according to dosage to the tumor:

(1) Less than 1,000 tissue r.
(2) 1,000–1,990 tissue r.
(3) 2,000–2,490 tissue r.
(4) 2,500 tissue r or more.

The earlier cases were treated with a 200 kv.p. mechanically rectified General Electric machine with a filter of 1 mm. copper plus 1 mm. aluminum, the half value layer being 1.4 mm. copper. The later cases were treated with a 220 kv.p. self-rectifying Maximar with 1 mm. copper plus 1.2 mm. aluminum, the half value layer being 1.7 mm. copper. Earlier cases were treated only through anterior and posterior fields. Later, lateral fields were added. The present technic involves the use of one anterior field approximately 20 × 20 cm., a right and left posterior oblique field, approximately 13 × 20 cm., and 2 lateral fields, about 12 × 20 cm. In the first group, 1 patient out of 10 survived four years; in the second group 8 out of 59 survived four years or more; and in the third group, 4 out of 24. The cases

TABLE III: CARCINOMA OF BLADDER: RESULTS WITH VARIOUS TYPES OF TREATMENT

Type of Treatment	Total No. of Cases	No. of Cases 1/1/30 to 12/31/35	Five-Year Survival of Cases 1/1/30–12/31/35
Fulguration only	23	15	2
Fulguration and radon	10	7	2
Fulguration and x-rays	18	11	2
Fulguration, radon, and x-rays	11	10	1
X-rays only	24	11	0
X-rays and radon	9	7	0
Resection only	16	5	1
Resection and radon	2	1	0
Resection and x-rays	13	..	.
Resection, radon, and x-rays	7	2	0
Partial cystectomy	1	1	1
Ureterostomy, cystectomy, and x-rays	1	..	.
Miscellaneous treatment (palliative)	4	..	.
No treatment	7	..	.

in group 4 were all treated in 1938 and 1939, and are therefore too recent for comparison. Most of these patients are already dead, and the results will be no better in this group than in the others. It therefore seems that increasing the dosage within the above limits has not been of great value.

Table II and Figure 2 (*a*) summarize the results in all our cases of carcinoma of the bladder, irrespective of type, survivals being dated from the first treatment at the University Hospital. Only 12.8 per cent survived five years. Figure 2 shows also the proportions of survivorship. The discrepancy in the four-year survivals (28 per cent) is due to the fact that the number of cases is too small for absolutely correct statistics, but since the rest of the curve follows a definite pattern, it seems reasonably accurate. In addition to the five-year survivals, there were 12 cases which were followed more than three years and found free of carcinoma. Some of these were among the earlier patients subsequently lost but well when last seen. In addition, there was one patient who died of pneumonia four years after the first treatment and who had, at autopsy, no evidence of carcinoma. If these 13 cases are considered as probably cured, the upper limit for possibly cured patients would be 31.4 per cent.

Fig. 2. Survival curves for 146 cases of carcinoma of the bladder.

A word of explanation is offered relative to the survival curves shown in Figures 2 and 3. Table II, for example, shows the number of cases for each year in the first column. The next column shows the number of patients alive one year later (61 of 146 original cases). This gives a one-year survival rate of 41.8 per cent, as shown in Figure 2 (*a*). At the end of two years, 43 were alive. The cases treated in 1939, however, cannot be used for two-year sur-

vivals because they were not followed long enough (this investigation was started in 1940). Thus, our two-year survivals are 43 of 131 cases. The fact that the curve goes down to the base line does not mean that all our patients are dead. It means that we have no known survivals of more than seven years. Figure 2 (*b* and *c*) and Figure 3 were similarly computed from the appropriate tables.

114 are dead and 5 have been lost, leaving a total of 18.5 per cent known to be alive.

Table IV and Figure 2 (*b* and *c*) show the difference in survival rates of papillary carcinoma and the infiltrating type. The five-year survival rate in the papillary group is 21.4 per cent as compared with only 7.1 per cent in the infiltrating type.

Table V and Figure 3 (*a* and *b*) show the survival rates in cases without metastases

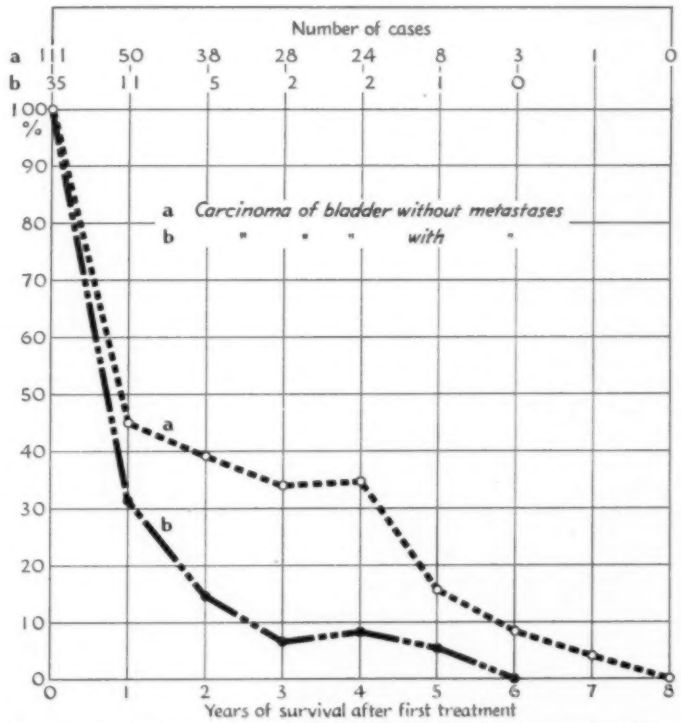

Fig. 3. Survival curves for carcinoma of the bladder with and without metastases.

Table III shows the type of treatment given, the total number of cases receiving such treatment, the number treated in the manner stated in the table from Jan. 1, 1930, through 1935, and the five-year survivals calculated from this latter group. It must be stated that all those who received x-ray treatment alone were practically hopeless when first seen. Of the total number of patients with carcinoma, as compared with those with metastases. It will be noted that the five-year survival rate in the former group is 15.7 per cent as compared with only 5.3 per cent in the latter.

A comparison of results at the University Hospitals with those reported by other authors is found in Table VI. These statistics were compiled from various articles and the five-year survival rate was

TABLE IV: RESULTS IN PAPILLARY AND INFILTRATING CARCINOMA OF THE BLADDER

Years	Cases	Years Survival									
		1	2	3	4	5	6	7	8	9	10
Papillary Carcinoma											
1930	2	1	1	1	1	1	0	0	0	0	0
1931	3 (1)	3	3	2	2	2	2	1	0	0	
1932	4	2	1	0	0	0	0	0	0		
1933	1	1	1	1	0	0	0	0			
1934	6 (1)	3	3	3	3	1	0				
1935	12 (5)	5	4	4	3	2					
1936	9 (2)	6	6	4	4						
1937	6 (1)	2	2	2							
1938	9 (1)	7	5								
1939	5	2									
Infiltrating Carcinoma											
1930	4 (2)	1	1	0	0	0	0	0	0	0	0
1931	4 (1)	2	1	1	1	1	0	0	0	0	
1932	5 (2)	2	0	0	0	0	0	0	0		
1933	10 (2)	3	3	3	3	1	1	0			
1934	8 (2)	2	0	0	0	0	0				
1935	11 (3)	6	5	5	5	1					
1936	14 (3)	5	4	4	4						
1937	13 (5)	4	2	0							
1938	10 (3)	2	1								
1939	10 (1)	2									

Figures in parenthesis represent cases with metastases.

TABLE V: RESULTS IN CARCINOMA OF THE BLADDER, WITH AND WITHOUT METASTASES

Years	Cases	Years Survival									
		1	2	3	4	5	6	7	8	9	10
Without Metastases											
1930	4	1	1	1	1	1	0	0	0	0	0
1931	5	3	2	2	2	2	2	1	0	0	
1932	7	3	1	0	0	0	0	0	0		
1933	9	4	4	4	3	1	1	0			
1934	11	3	2	2	2	1	0				
1935	15	11	9	9	8	3					
1936	18	10	9	8	8						
1937	13	5	4	2							
1938	15	7	6								
1939	14	3									
With Metastases											
1930	2	1	1	0	0	0	0	0	0	0	0
1931	2	2	2	1	1	1	0	0	0	0	
1932	2	1	0	0	0	0	0	0	0		
1933	2	0	0	0	0	0	0	0			
1934	3	2	1	1	1	0	0				
1935	8	0	0	0	0	0					
1936	5	1	1	0	0						
1937	6	1	0	0							
1938	4	2	0								
1939	1	1									

TABLE VI: CARCINOMA OF BLADDER: COMPARISON OF VARIOUS SERIES

Author	No. of Cases	Type of Treatment	Percentage Five-Year Survival
E. E. Ferguson (18)	130*	Various types and combinations	10.45%
A. L. Dean and J. Balfour (14)	50 consecutive papillary	Radon and x-rays	54.0 %
	50 consecutive infiltrating	Radon and x-rays	14.0 %
Barringer (4)	214	Radon and occasionally radium	33.1 %
Watson and Herger (27)	129 papillary	Various types	28.0 %
	50 infiltrating	Various types	12.0 %
J. T. Farrell and T. R. Fetter (17)	72	Various types	4.1 %
Orr, Carson, and Novak (24) and Butler (9)	Quote the Carcinoma Registry as giving		23.0 %
Authors' series	146	Various types	12.8 %
	57 papillary	Various types	21.4 %
	89 infiltrating	Various types	7.1 %

* Of these 130 cases, 70 were of the infiltrating type and in these the five-year survival rate was only 4.2 per cent

calculated as nearly as possible on the same basis as that on which our own was determined. Highly selected groups are not included in this table.

CONCLUSIONS

1. Various data relative to tumor of the bladder have been presented.

2. The delay of treatment for carcinoma (2.3 years) could be materially reduced by increased co-operation of the physicians and education of the public. The toll of carcinoma of the bladder may thus be considerably reduced.

3. Hematuria, which is the commonest first symptom, demands serious consideration in every instance in which it occurs.

4. The results of the treatment of carcinoma of the bladder are not good.

5. With careful attention to detail, the results may be improved with radon and radium therapy in suitable cases.

6. Contact and possibly supervoltage x-ray therapy may prove of value.

7. External irradiation has not been as effective as was previously thought, especially in doses of less than 3,000 tissue r to the tumor.

8. Metastases appear more frequently than is generally believed and should be diligently sought if a radical surgical procedure is contemplated.

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Effect of Combined Fever and X-Ray Therapy on Far-Advanced Malignant Growths[1]

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AS FAR BACK AS 1935, Warren (1) noted that there was evidence of intensification of the destructive effect on malignant cells if fever therapy were combined with irradiation. Delario (2) in the same year reported that, when rats bearing Flexner-Jobling sarcoma were treated simultaneously with radiothermy and with x-rays, the number of tumors disappearing was greater than with any other method of therapy tried.

Doub (3), in 1935, reported a case of osteogenic sarcoma of the clavicle treated with radiation and fever therapy. Noting that the use of Coley's toxins had usually been followed by an elevation of temperature, he was inclined to feel that any beneficial effect of this treatment might be due to the febrile reaction. He administered four series of deep x-ray therapy at intervals of two months, with fever therapy at weekly intervals for eight weeks. It was his opinion that the fever therapy rendered the tumor cells more radiosensitive. His patient improved clinically and roentgenologically and was in good condition and working a year and a half after the institution of treatment.

Overgaard (4), in 1936, working with white mice bearing implanted tumors, demonstrated a healing influence of short and ultra-short waves. No x-ray therapy was administered, the favorable results being attributable solely to the heat applications.

Fuchs (5) reported in 1936 the treatment of two cases of bronchogenic carcinoma with two to three hours of diathermy in an attempt to sensitize the tumor cells to x-rays. No convincing evidence of any beneficial effects was noted.

Warren (6), writing again in 1936, concluded, following preliminary investigations on the combined effects of fever and roentgen radiation upon animal tissues, that "it is our definite impression from the animal experimental work and from the few patients that have co-operated with us in these studies that the effectiveness in destroying the tumor is greatly enhanced when fractional roentgen therapy is combined with fever therapy in the proper manner."

Berkman and Dessauer (7) reported (1937) some improvement in hopeless cancer cases treated by a combination of diathermy and x-ray therapy. Korb (8) used local short-wave hyperthermia before, during, and after x-ray treatment but made no statement as to whether benefits had been observed.

Jares and Warren (9), in 1939, demonstrated that "temperatures of 41.5 and 42.0° C. are capable of damaging or destroying mouse sarcoma 180, rat carcinoma 256, Jensen rat sarcoma, and the Brown-Pearce rabbit epithelioma *in vitro* after appropriate periods of exposure."

Overgaard and Okkels (10), experimenting with a transplantable mouse sarcoma (Wood's sarcoma), found (1940) that heat had a specific tumor-destroying effect. Following this observation they performed a second series of experiments utilizing combined heat and roentgen therapy and observed a decided increase in cures in those animals given heat treatment before irradiation. They also noted that the combination of heat and x-rays, each in doses considered therapeutically ineffective, resulted in complete cures in many

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TABLE I: CARCINOMA OF CERVIX

Case No. Age Date Stage*	Combined Fever and X-Ray Therapy	Irradiation Alone	Pathologic Diagnosis	Status of Patient
1 40 yrs. 11/4/40 IV	6/27/41: Rt. and left ant. pelvis, 300 r to each area	1/27/41–2/14/41: Rt. and left ant. and post. pelvis, 1,050 r to each area	Squamous-cell carcinoma	Living; improved
2 49 yrs. 7/11/41 III	7/22/41: Rt. and left ant. pelvis, 300 r to each area 7/30/41: Rt. and left ant. pelvis, 300 r to each area 8/15/41: Rt. and left post. pelvis, 300 r	7/23/41–8/7/41: Rt. and left post. pelvis, 1,500 r; left post. pelvis, 1,500 r	Squamous-cell carcinoma	Living; improved
3 49 yrs. 7/13/41 III	7/25/41: Rt. and left ant. pelvis, 300 r 8/7/41: Rt. and left post. pelvis, 400 r	7/28/41–8/12/41: Rt. and left post. pelvis, 900 r; rt. and left ant. pelvis, 600 r	Squamous-cell carcinoma	Living; improved
4 49 yrs. 5/9/41 IV	5/12/41: Rt. and left ant. pelvis, 300 r	5/13/41–6/10/41: Rt. and left post. pelvis, 1,500 r; rt. and left ant. pelvis, 1,200 r 6/11/41: 5,760 mg.-hr. radium	Squamous-cell carcinoma	Living; marked improvement
5 58 yrs. 12/20/40 III	8/4/41: Rt. and left ant. pelvis, 300 r 8/15/41: Rt. and left post. pelvis, 300 r	2/20/41–3/21/41: Rt. and left ant. and post. pelvis, 1,500 r 10/3/41: 2,880 mg.-hr. radium	Squamous-cell carcinoma	Living; slight improvement
6 42 yrs. 8/19/41 III	9/9/41: Rt. and left ant. pelvis, 350 r	9/6/41–10/10/41: Rt. and left post. pelvis, 1,500 r; left ant. pelvis, 1,200 r; rt. ant. pelvis, 1,500 r 10/31/41: 2,340 mg.-hr. radium	Squamous-cell carcinoma	Living; slight improvement
7 29 yrs. 10/22/41 III	10/28/41: Rt. and left ant. pelvis, 300 r	10/30/41: present	Squamous-cell carcinoma	Living; improved
8 52 yrs. 10/1/41 II	10/17/41: Rt. and left ant. pelvis, 300 r	10/14/41: present	Squamous-cell carcinoma	Living
9 67 yrs. 2/21/41 III	3/4/41: Pubic and lower lumbar fields, 300 r	2/24/41–2/26/41: Rt. and left ant. pelvis, 300 r; rt. and left post. pelvis, 150 r	Squamous-cell carcinoma	Deceased; tumor improved
10 32 yrs. 2/4/41 IV	2/19/41: Rt. lat. hip, 750 r		Squamous-cell carcinoma	Deceased; no improvement
11 37 yrs. 1/3/41 IV	2/4/41: Ant. and post. lower pelvis, 750 r 2/25/41: Rt. and left lat. pelvis, 748 r	3/15/40–4/22/40: Rt. and left ant. pelvis, 2,823 r 3/26/40: 4,338 mg.-hr. radium 4/14/41–4/28/41: Rt. and left oblique pelvis, 1,200 r	Squamous-cell carcinoma	Deceased
12 27 yrs. 10/8/40 II	3/18/41: Rt. and left ant. pelvis, 300 r	10/16/40: 4,455 mg.-hr. radium 11/18/40–1/16/41: Rt. and left ant. and post. pelvis, 1,800 r; rt. and left lateral pelvis, 1,500 r 3/19/41–3/20/41: Rt. and left post. pelvis, 300 r	Squamous-cell carcinoma	Deceased

* League of Nations classification.

TABLE II: CARCINOMA OF BREAST

Case No. Age Date Diagnosis	Combined Fever and X-Ray Therapy	Irradiation Alone	Pathologic Diagnosis	Status of Patient
13 F. 43 yrs. 6/20/41 Sweat - gland carcinoma	6/26/41: Rt. breast, ant., 400 r	6/24/41–6/25/41: Upper and lower rt. breast, 300 r 6/30/41–7/18/41: Post. rt. axilla, 1,700 r; lower rt. breast, 950 r; upper rt. breast, 900 r		Living; ulceration healed and then broke down
14 M. 66 yrs. 1/24/41 Scirrhous carcinoma	11/8/40: Rt. axilla, 720 r	2/4/38–3/3/38: Rt. ant. breast, 2,049 r; rt. scapula, 1,504 r; rt. axilla, 1,744 r	Carcinoma	Living; 75 per cent reduction of node in right axilla
15 F. 46 yrs. 3/7/41 Metastases to liver	3/21/41: Rt. and left abdomen, 300 r 3/25/41: Rt. and left abdomen, 300 r	3/26/41–5/1/41: Rt. and left lateral abdomen, 1,800 r; left lumbar region, 1,500 r; rt. lumbar region, 1,200 r		Living; improved
16 F. 55 yrs. 9/19/41 Postoperative recurrence	9/24/41: Left ant. chest, 750 r		Carcinoma	Living; improved
17 F. 39 yrs. 10/13/40 Scirrhous carcinoma	3/19/41: Rt. ant. and post. chest, 300 r	10/16/40–11/12/40: Upper rt. chest, 1,300 r; rt. lower breast, 1,250 r; post. axilla, 1,200 r 1/20/41–1/22/41: Post. axilla, 450 r; upper rt. breast, 300 r; lower rt. breast, 150 r 3/20/41–4/15/41: Rt. post. chest, 1,350 r; upper and lower rt. chest, 1,050 r	Scirrhous carcinoma	Living; pleural effusion; metastases to liver (?)
18 F. 63 yrs. 1/23/40 Ulcerated carcinoma	3/5/40: Rt. breast and axilla, 605 r 3/14/40: Rt. post. scapula, 800 r	1/31/40–2/12/40: Rt. breast and axilla, 3,918 r	Scirrhous carcinoma	Deceased; ulceration healed completely; nodes disappeared
19 F. 47 yrs. 6/12/40 Scirrhous carcinoma	6/18/40: Rt. breast and axilla, 750 r	6/14/40–7/12/40: Rt. breast, 2,138 r; rt. axilla, 1,844 r		Deceased; bony metastases developed
20 F. 57 yrs. 5/19/40 Scirrhous carcinoma	5/26/41: Rt. breast, ant., 300 r	5/28/41–6/10/41: Post. axilla, 1,200 r; upper rt. breast, 600 r; lower rt. breast, 750 r 10/14/41–11/7/41: Upper rt. chest, 1,350 r; lower rt. chest, 1,500 r; axilla, 1,800 r	Scirrhous carcinoma	Living; improved
21 F. 39 yrs. 6/7/39 Ulcerated carcinoma	4/4/41: Left breast, 400 r	6/20/39–7/12/39: Left ant. chest, 3,800 r 7/12/39–7/19/39: Tumor of left breast, 1,500 r 7/30/40–8/6/40: Topical radium, 500 mg.-hr. 4/8/41–4/11/41: Left breast, 800 r		Living; improved
22 F. 42 yrs. 10/29/41 Scirrhous carcinoma	10/2/40: Left lat. chest, 750 r	11/8/39–11/21/39: Rt. lat. breast, 1,200 r; ant. and post. chest, 900 r; rt. parasternal area, 900 r 2/28/40–12/29/40: 6 series x-ray tr. to various metastatic areas	Scirrhous carcinoma	Deceased; metastases to skeleton

of their animals. It did not appear to make any particular difference whether the heat treatment was given before or after irradiation.

Sugiura (11) obtained regression of mouse sarcoma after treatment by x-rays followed by repeated exposure to ultra-short radio waves. He also studied the combined effects of x-rays and lowering of temperature (freezing) but observed no beneficial effect from this procedure.

Combined fever and x-ray therapy was first begun by the authors at George W. Hubbard Hospital of Meharry Medical College in the summer of 1939 (12). In the belief that such methods should first be utilized on cases deemed non-operable, a series of 42 advanced, inoperable tumors, in patients ranging from 23 to 71 years of age, has been studied and constitutes the basis of this report.

It was the impression of the authors that, if fever plays a significant rôle in increasing the sensitivity of tumor cells, either through an increased metabolic rate or through dehydration of tumor tissues, the logical procedure would be to administer the radiation at the time of greatest physiological disturbance, namely immediately after completion of fever therapy. Consequently the procedures utilized in this series have included a preliminary preparation for fever therapy, involving an increase of fluid and chloride intake, fever therapy, and x-ray therapy administered immediately upon completion of the fever treatment while the hyperpyrexia was present.

Each case has been carefully studied by the service to which it was admitted. The cases have been presented before the hospital tumor clinic for consultation as to the procedure best adapted to each. Whenever a case has been considered operable, it has been referred to the proper service for surgical procedures and also to the department of radiology for preoperative and postoperative therapy as indicated. Cases considered inoperable by the tumor clinic consultants have then come under the supervision of the departments of radiology and medicine. Biopsy material is obtained by the surgical staff and examined in the department of pathology.

The department of medicine has assumed the responsibility of preparing the patients for fever therapy, by adequate fluid and chloride administration, so as to avoid possible chloride deficiency reactions during or following the treatment.

Fever therapy has been given in a fever cabinet, with the patient on an air-water rubber mattress placed over the heating element. The humidity of the cabinet is controlled by a small vaporizer. The patient's temperature can constantly be observed by means of a thermocouple inserted into the rectum and connected with an electrical recording thermometer. Since the temperature of the patient is largely controlled by the cabinet humidity, the heated mattress and cabinet temperature rarely exceeds 100° F. even when the body temperature is elevated to 106 or 107° F.

It requires from one and a half to three hours to obtain the desired temperature. Depending upon the condition of the patient and his reactions, the temperature is raised to 104–106° F. The maximum temperature elevation desired is maintained in the cabinet for thirty to sixty minutes. The patient is then transferred to the x-ray therapy room. It is important that he be fully protected by blankets during this transfer and that the x-ray treatment room be warm and free from drafts. The patient is kept well wrapped, except for the portion of the body exposed to x-rays, during the radiation procedure.

The technical factors used in administration of the deep x-ray therapy are as follows: Old drum type of machine; 200 kv. p.; 0.5 to 1.0 mm. Cu filtration; 50 cm. distance in the majority of the cases, 60 cm. in a few; 0.9 mm. Cu H.V.L.; 17 r/m flux; 5 ma. The size of the fields depends upon the lesion treated. Recently a more modern type of unit at 220 kv. p. has been used, at 20 ma., 50 r/m flux, 50 cm. distance, and 0.5 mm. Cu filtration. The H.V.L. for this new unit is 1.0 mm. Cu, with the above filtration. All x-ray dosages are measured in air.

TABLE III: OSTEOGENIC SARCOMA AND MYXOSARCOMA

Case No. Age Date Diagnosis	Combined Fever and X-Ray Therapy	Irradiation Alone	Pathologic Diagnosis	Status of Patient
23 F. 40 yrs. 10/2/41 Osteogenic sarcoma, rt. knee	10/8/41: Rt. knee, med. and lat., 750 r 10/14/41: Rt. knee, ant. and post., 750 r 10/20/41: Rt. knee, med. and lat., 400 r	10/27/41–10/31/41: Rt. knee, ant. med. and lat., 200 r to each area (400 r)	None	Living; 60 per cent reduction of mass
24 M. 40 yrs. 8/6/40 Osteogenic sarcoma, left arm	8/9/40: Left arm, ant. and post., 750 r	9/9/40–10/14/40: Rt. lower ribs, ant., 650 r; rt. post. mid chest, 250 r; left knee, post., 200 r; rt. sacroiliac area, 297 r; rt. ant. chest, 200 r	None	Living; tumor completely disappeared; x-ray evidence of healing
25 F. 30 yrs. 10/24/39 Osteogenic sarcoma, left arm	12/13/39: Left arm, ant. and post., 483 r	11/10/39–12/4/39: Left arm, ant., 1,563 r; left arm, post., 1,424 r	Osteogenic sarcoma	Living; complete bony healing; clinically cured
26 M. 46 yrs. 10/3/41 Osteogenic sarcoma, rt. arm	10/9/41: Upper half rt. arm, ant. and post., 750 r 10/15/41: Rt. arm, med. and lat., 400 r 10/22/41: Rt. arm, ant. and lat., 400 r		Osteogenic sarcoma	Living; mass completely disappeared
27 M. 41 yrs. 9/19/41 Myxosarcoma, left leg	9/25/41: Left popliteal region, 750 r	9/26/41–9/30/41: Left popliteal region, post., 900 r	Myxosarcoma	Living; improved
28 F. 23 yrs. 7/10/40 Myxosarcoma, left leg	7/15/41: Left inguinal region and rt. breast, 500 r to each area	7/10/40–8/1/40: Ant., post., and lat. left inguinal region, 2,310 r each area 7/9/41–7/14/41: Rt. and left shoulder, rt. breast, left arm, and left inguinal region, 300 r each area 7/15/41–9/12/41: Rt. breast, 990 r; rt. shoulder, 1,210 r; left shoulder, 1,320 r; rt. inguinal region, 1,540 r; rt. knee, 5,620 r	Myxosarcoma	Living
29 F. 37 yrs. 8/7/41 Myxosarcoma, rt. thigh	8/14/41: Rt. ant. thigh, 500 r 8/19/41: Rt. lat. thigh, 400 r	9/4/41–9/12/41: Rt. ant. thigh, 2,400 r; lat. rt. thigh, 1,900 r; med. and post. rt. thigh, 600 r each area	Myxosarcoma	Living; tissue mass markedly reduced

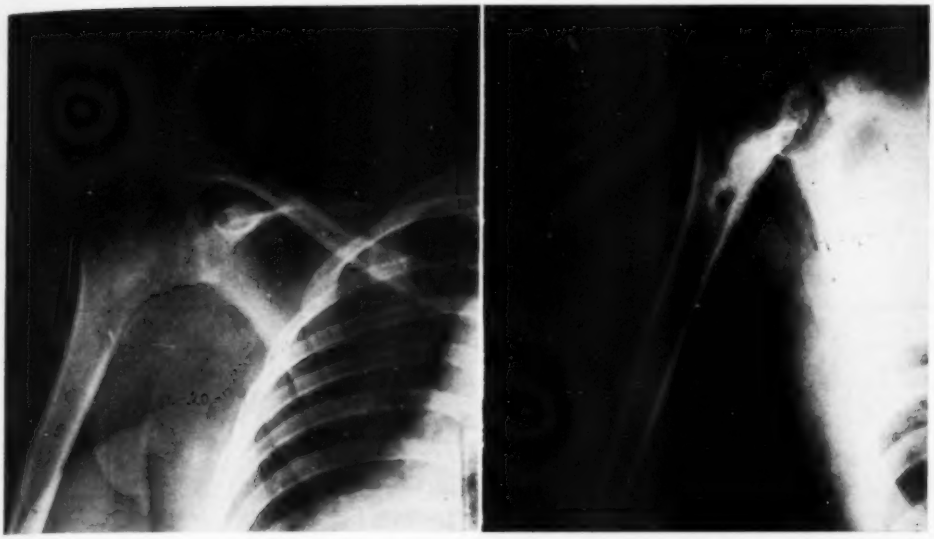
The accompanying tables indicate the types of malignant tumors treated, the method, amount of irradiation, pathological diagnosis, and present status of the patient. A few case histories are outlined.

CASE REPORTS

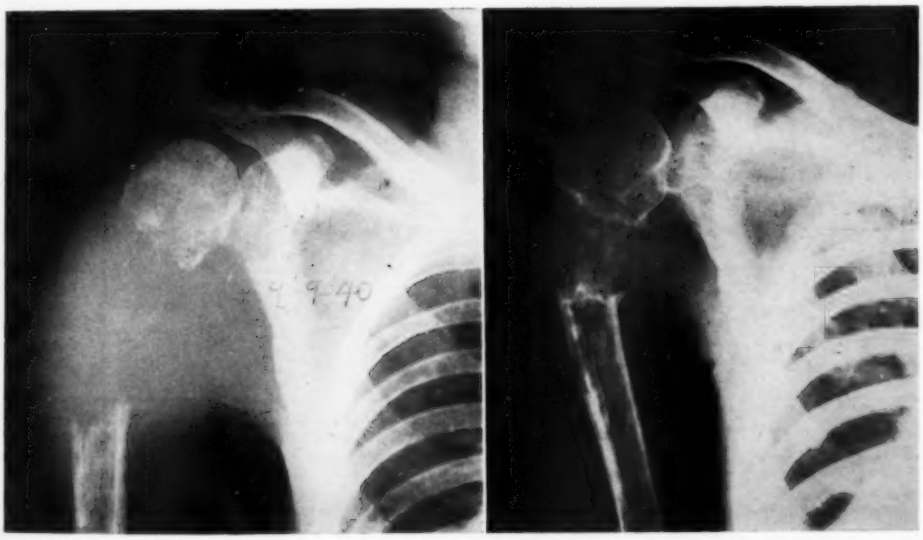
CASE 25: M. M., female patient, age 30 years, was first seen in August 1939, complaining of pain in the left shoulder and arm. The x-ray and biopsy diagnosis was osteogenic sarcoma of the left humerus (Fig. 1).

Following combined fever (104° F.) and x-ray therapy (approximately 4,000 r) the patient gained 35 pounds in weight, and at the time of this report is in excellent health, with complete restoration of the left humerus (Fig. 2).

CASE 24: S. B., male patient, age 40 years, was first seen in August 1940, complaining of pain in the left arm and chest. X-ray examination showed



Figs. 1 and 2. Case 25: Osteogenic sarcoma of the humerus before and after combined fever and roentgen therapy.



Figs. 3 and 4. Case 24: Soft-tissue tumor of the humerus with metastases in the ribs, before and after combined fever and roentgen therapy.

marked destruction of the upper third of the left humerus, with a large soft-tissue tumor of this area (Fig. 3) and metastatic lesions in the ribs.

The patient was given fever therapy (106° F.) with x-ray therapy (1500 r) over the arm and shoulder, and over the ribs. He gained over 30 pounds weight, and gradual bridging and restoration of the left humerus (Fig. 4) and complete healing of metastatic deposits in the ribs followed. He is now well and working.

CASE 39: J. B., male, age 57 years, was admitted June 6, 1941, with a diagnosis of bronchogenic carcinoma of the right lower lobe, based on x-ray and bronchoscopic examination and pathological study of biopsy material. There was atelectasis of the right lower lobe with a mediastinal shift to the right.

TABLE IV: MISCELLANEOUS TUMORS

Case No. Age Date Diagnosis	Combined Fever and X-Ray Therapy	Irradiation Alone	Pathologic Diagnosis	Status of Patient
30 M. 55 yrs. 10/11/41 Carcinoma of rt. kidney	7/7/41: Ant. and post. rt. hypochondriac region, 300 r; post. rt. lumbar region, 500 r	11/22/40–1/16/41: Ant., post., and lat. rt. lumbar regions, 2,600 r 7/7/41–9/3/41: Left post. lumbar region, 900 r.; rt. axilla, 1,400 r; rt. lat. lumbar region, 1,650 r	Renal-cell carcinoma	Living; improved
31 F. 52 yrs. 1/27/41 Melanosarcoma of left foot with metastases to entire left lower extremity	2/6/41: Ant. and post. left inguinal region, 748 r 2/13/41: Left med. thigh, 748 r 3/11/41: Left lat. thigh, 720 r 4/10/41: Left leg, 748 r	Superficial x-ray therapy 2/10/41–4/4/41: Left foot (plantar), 4,000 r (divided dose) 3/27/41: Left lat. foot, 500 r 4/4/41: Left knee, med., 510 r	Melanosarcoma of foot	Deceased; inguinal mass much smaller
32 F. 67 yrs. 8/29/41 Carcinoma of stomach	9/2/41: Ant. abdomen, 750 r			Living; no improvement
33 M. 71 yrs. 5/29/41 Melanosarcoma of left axilla	6/3/41: Left axilla, 750 r	6/11/41–7/17/41: Ant. left axilla, 150 r; left ant. breast, 900 r; post. left axilla, 600 r	Melanosarcoma	Living; no recurrence
34 F. 70 yrs. 11/15/40 Adenocarcinoma of corpus uteri	11/30/40: Ant. uterus, 700 r 12/9/40: Rt. lower quadrant, 300 r	11/30/40–1/9/41: Rt. and left pelvis, ant. and post., 1,500 r; post. lumbar region, 900 r	Adenocarcinoma of corpus uteri	Living; marked reduction in tumor
35 M. 39 yrs. 10/1/41 Melanosarcoma of rt. foot with metastases to rt. lower extremity	10/10/41: Rt. med. foot and rt. inguinal area, ant., 750 r 10/16/41: Rt. ant. thigh, 750 r 10/23/41: Rt. knee, med., 600 r	10/27/41–11/13/41: Rt. leg and knee, 300 r to each area; rt. thigh and rt. lat. abdomen, 600 r; rt. inguinal region, 200 r	Melanosarcoma	Living; no change except for decrease in sensitivity of skin
36 M. 60 yrs. 6/25/41 Carcinoma of bladder	7/9/41: Ant. bladder, 750 r 7/31/41: Ant. bladder, 400 r	7/9/41–8/12/41: Post. gluteal region, 2,700 r; post. rt. gluteal region, 2,400 r	Papillary adenocarcinoma of bladder	Living; 75 per cent shrinkage of tumor
37 M. 36 yrs. 6/26/41 Retroperitoneal metastases from seminoma of testis	7/29/41: Ant. rt. abdomen, 500 r 8/8/41: Ant. rt. abdomen, 300 r 9/9/41: Post. rt. abdomen, 750 r	7/29/41–9/9/41: Ant. rt. abdomen, 1,200 r; post. rt. abdomen, 1,500 r; lat. rt. abdomen, 900 r	Retroperitoneal metastases from seminoma of testis	Living; tumor in abdomen completely disappeared
38 F. 60 yrs. 8/13/41 Carcinoma of rectum	8/13/41: Left lat. pelvis, 300 r	8/14/41–8/19/41: Rt. and left lat. pelvis, 600 r	Adenocarcinoma	Deceased; no apparent effect on tumor

TABLE IV: MISCELLANEOUS TUMORS—*Continued*

Case No. Age Date Diagnosis	Combined Fever and X-Ray Therapy	Irradiation Alone	Pathologic Diagnosis	Status of Patient
39 M. 57 yrs. 6/20/41 Carcinoma of lung	6/21/41: Ant. rt. lower chest, 399 r; post. rt. lower chest, 399 r. Temp.: 106° F. at beginning and 104° F. at end of treatment 7/2/41: Post. rt. lat. chest, 300 r; rt. ant. chest, 300 r. Temp.: 105° F. at beginning of treatment 7/8/41: Ant. rt. chest, 200 r; post. rt. chest, 200 r. Temp.: 102.8° at beginning of treatment 7/11/41: Left oblique ant. chest, 241 r. Temp.: 103.8° F. at beginning and 103° F. at end of treatment	6/23/41–7/23/41: Rt. ant. chest, 1,100 r; rt. post. chest, 800 r; left lat. post. chest, 300 r; left ant. lat. chest, 1,500 r; left post. chest, 1,200 r	Bronchogenic carcinoma	Living; tumor almost completely disappeared
40 M. 71 yrs. 5/1/41 Carcinoma of prostate	5/1/41: Post. rt. lat. pelvis, 300 r; post. left lat. pelvis, 300 r. Temp.: 104.8° F. at beginning and 103° F. at end of treatment 5/16/41: Left post. pelvis, 300 r; rt. post. pelvis, 300 r. Temp.: 103° F. at beginning and 102° F. at end of treatment	5/6/41–10/11/41: Left post pelvis, 1,500 r; rt. post. pelvis, 1,200 r; left ant. pelvis, 1,200 r; left oblique pelvis, 600 r; rt. lat. pelvis, 300 r; rt. gluteal region, oblique, 300 r; rt. ant. pelvis, 1,500 r	Not obtained	Living; improved
41 M. 52 yrs. 2/24/41 Carcinoma of stomach	3/3/41: Rt. ant. abdomen, 300 r; left ant. abdomen, 300 r. Temp.: 103.8° F. at beginning and 101.2° F. at end of treatment	3/5/41–3/28/41: Post. rt. lower abdomen, 750 r; ant. rt. lower abdomen, 750 r; ant. rt. upper abdomen, 600 r; ant. left lower abdomen, 450 r; ant. left upper abdomen, 600 r; post. rt. upper abdomen, 750 r; post. left upper abdomen, 450 r	Not obtained	Deceased; no improvement
42 F. 40 yrs. 7/11/41 Carcinoma of vulva	7/28/41: Ant. left inguinal region, 500 r; ant. rt. inguinal region, 500 r. Temp.: 106° F. at beginning and 102° F. at end of treatment 8/6/41: Ant. rt. inguinal region, 400 r; ant. left inguinal region, 400 r. Temp.: 106.4° F. at beginning and 100.3° F. at end of treatment	7/30/41–9/12/41: Post. left gluteal region, 2,100 r; post. rt. gluteal region, 1,800 r; ant. rt. inguinal region, 300 r; ant. left inguinal region, 600 r; left lat. pelvis, 2,130 r	Epidermoid carcinoma	Living with disease

Fever therapy (106, 105, and 103° F.) was given followed by x-ray therapy (2,100 r to the anterior right lower chest, 1,800 r to the posterior right lower chest, 1,741 r to the left lateral chest, and 1,200 r to the posterior left lateral chest). Marked tumor shrinkage was obtained. Progress was complicated by a sterile empyema, necessitating a rib resection. The mediastinal contents reshifted and there was almost complete disappearance of tumor. The patient is living at the present time.

CASE 18: M. T., female patient, age 63 years, was admitted to the hospital Feb. 2, 1940, complaining of a "bad breast." She gave a history of right breast tumor for at least seven months with ulceration for the past two months. A huge ulcer was present and the right axilla was filled with metastatic nodules. The pathological diagnosis was scirrhous carcinoma.

Fever therapy (104° F.) combined with x-ray therapy (1,400 r) brought about marked improve-

TABLE V: SUMMARY OF EFFECTS OF COMBINED FEVER AND X-RAY THERAPY ON 42 CASES OF ADVANCED MALIGNANT NEOPLASMS

Type of Case	Total Number	Living	Dead
Carcinoma			
Breast	10	7	3
Cervix	12	8	4
Sarcoma			
Osteogenic	4	4	0
Myxosarcoma	3	3	0
Melanosarcoma	3	2	1
Miscellaneous	10	7	3
Totals	42	31	11
Percentage improved.....65%			

ment, with healing of the ulcerated breast and disappearance of axillary nodules. The patient died of a cerebral accident in September 1941.

CASE 36: W. J., male patient, age 60 years, was admitted to the hospital June 21, 1941, complaining of "passing blood from the urinary tract." He was markedly anemic. Cystoscopic examination showed a papillary tumor, and biopsy led to a diagnosis of papillary adenocarcinoma.

Combined fever (103.2° F.) and x-ray (6,200 r) therapy was followed by a 75 per cent regression of the tumor and complete disappearance of symptoms. The patient returned to his work.

SUMMARY AND CONCLUSIONS

A review of the available literature on heat therapy combined with x-ray irradiation in the treatment of experimental cancer and a small number of hopeless malignant tumors has been given. The technic used in the treatment of a group of 42 far advanced inoperable cases of malignant growth of various types in the tumor clinic of George W. Hubbard Hospital of Meharry Medical College has been outlined. With this method of combined fever and x-ray therapy there has been no mortality directly attributable to the treatment. Tables summarizing the cases are presented together with reports of two osteogenic sarcomas, one bronchogenic carcinoma, one ulcerating scirrhous carcinoma of the breast, and an adenocarcinoma of the urinary bladder.

There has been symptomatic improvement in 65 per cent of this group (27 of the 42 patients). Unquestionable evidence of regression of the primary growth and of metastatic lesions has been obtained.

The results have led the authors to feel that there are potentialities in the use of combined fever and x-ray therapy that are not present in the use of x-ray therapy alone. It is felt, furthermore, that there has been sufficient basic experimental work performed by competent investigators on the use of fever and x-ray therapy to justify the careful use of these combined procedures in man.

Although our series represents a miscellaneous group of malignant tumors, it is our impression that the most satisfactory results have been in the treatment of sarcoma.

No statement as to cure is being made by those of us who have been performing this type of experimental therapy. It will require many years of careful follow-up and observation to obtain adequate evidence for or against the curative possibilities of the method. However, in view of the improvement observed in our studies on hopelessly inoperable cases, it is suggested that it would be desirable to investigate the effects of similar procedures in conjunction with surgical measures on operable cases. It is conceivable that the combined use of fever and x-ray therapy with surgical measures might improve the present survival statistics for surgery alone, or for surgery combined with preoperative and postoperative irradiation without fever therapy.

It is the hope of the authors that similar studies will be undertaken by other investigators so that the procedures outlined in this paper may be more fully evaluated.

Doctors Building
Nashville, Tenn.

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DISCUSSION

Henry J. Ullmann, M.D. (Santa Barbara, Calif.): It is, of course, impossible to discuss a paper intelligently when one knows nothing whatever of the subject. But the new things should be discussed, as well as the old. There is a theoretical possibility of benefit from the addition of heating to radiation because of the acceleration of reactions at increased temperatures, although there is some discrepancy in the reports to date. But in treating the body as a whole with fever therapy plus radiation, one changes its metabolic processes very definitely, as was shown by Bischoff and his associates some years ago, and we must therefore consider the effect to be probably an effect on the tumor bed rather than an exhilaration of the physicochemical properties due to the increase in temperature. However, I need not go into these chemical changes. I would like to ask Doctor Shoulders if there have been any deaths from these treatments.

Dr. Shoulders (*closing*): We have actually improved several of these cases and we have had no deaths attributable to the method used.

Blood Findings in Cyclotron Workers[1]

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WITH THE increasing number of cyclotrons in operation and the wider use of radioactive compounds in quantities larger than for tracer work, the problem of possible dangers to the workers from radiation must be considered. The sources of danger are the neutrons themselves and the alpha, beta, or gamma radiation given off by the different targets used or by parts of the apparatus.

Two large groups of workers—those associated with the Harvard University cyclotron and those associated with the cyclotron and the electrostatic generator at the Massachusetts Institute of Technology—were studied; the Harvard University group through the co-operation of Drs. K. T. Bainbridge and Roger Hickman, and the Massachusetts Institute of Technology group through the co-operation of Prof. Robley D. Evans and Doctor Van der Graaf. Every effort has been made since the first to protect those working with these two cyclotrons and the generator. From time to time, however, certain almost unavoidable exposures arose in the handling of targets and in carrying out chemical manipulations on radioactive isotopes, as well as in the course of necessary repairs to the cyclotrons.

From our knowledge of the effects of radium and of x-rays, changes in the blood or damage to the skin or gonads were to be expected before damage to other tissues if radiation exceeded the limit of safety. Damage to the skin is usually obvious because of the acute response. It has not been encountered among these workers. Skin changes are most readily produced by beta radiation. For practical reasons gonadal changes could not be checked.

Evans (2) has called attention to the danger that may exist in the air from radioactive material and has investigated particularly the alpha radiation of radon and thorium B. Lung cancer may be induced by inhalation of radioactive substances. The safe limit is regarded as 10^{-11} curies per liter of air. Pulmonary exposure is not a hazard in cyclotron workers unless through the inhalation of particles such as might occur in sanding the dees (or electrodes). An attempt has been made to extrapolate alpha ray data to neutrons (Third International Cancer Congress, Atlantic City, N. J., 1939, Section on Biophysics).

Damage to the constituents of the blood may be very insidious. It has been long known that radium, radioactive substances, and x-rays will produce profound alterations in the blood, ranging from moderate anemia to leukemia (1). Moreover, repeated small exposures to radiation may cause more lasting damage in bone marrow than does a single large exposure (5). Regenerative hyperplasia of the marrow elements, reflected by elevated cell counts in the blood, is rarely seen except as a late result of repeated exposure to low intensity radiation (1). Thus, in the cyclotron workers, elevations in the white cell count unexplained by acute illness or injury have been considered as probable evidence of hyperplastic response to bone marrow injury.

Of special interest are the observations of Martland (4), who found in some cases of occupational poisoning from radium and mesothorium a normal blood picture but a bone marrow with marked hyperplasia and immaturity. In his cases, however, the source of radioactivity was deposited in the bones and hence in intimate and constant contact with the marrow cells. Usually the peripheral blood reflects with fair accuracy the condition of the bone marrow.

Dunlap (1) has collected 24 cases from the literature in which leukemia developed

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[1] From the Laboratories of Pathology of the Harvard Cancer Commission and of the New England Deaconess Hospital.

Read in part before the American Society for Experimental Pathology, April 3, 1942. Accepted for publication in May 1942.

following chronic exposure to radiation. The patients ranged in age from twenty-nine to fifty-three years. Four of the cases followed exposure to radioactive substances. The disease in these cases differed in no way from that of leukemia due to other causes. The other hazards of irradiation of the hematopoietic tissues, granulocytopenia and radiation anemia, have been adequately discussed by Dunlap and will not be considered here.

But few data are available on groups of workers. Blood studies were made on those engaged in the refining of radium and mesothorium (and hence exposed to repeated small doses of radiation) at the University of Missouri, where from 4 to 5 gm. were refined between 1930 and 1936 (6). Graduate students carried out the work. The workers handling material of high concentration frequently received burns of varying intensity on the thumb and index finger. Blood counts were made at frequent intervals and, while they varied from time to time, remained within the normal range. In the case of one worker who developed a slight anemia, complete recovery occurred after he discontinued the work.

METHODS AND OBSERVATIONS

Owing to the rapidly varying conditions of exposure in working about the cyclotrons and with their products, satisfactory measurements of the total exposure to radiation of any given worker could not be made. We can only say that it was usually minimal, and such safety factors as distance, protective water tanks, and other devices were used carefully. In the Technology group, the worker at the control bench received less than 1.5 r (or 0.2 n) per month, the worker changing targets less than 3 r per month.

Observations were started on the Harvard cyclotron workers Oct. 9, 1939, and on the Massachusetts Institute of Technology workers Oct. 17, 1939, and have continued, usually at monthly intervals, up to the present time. The counts were made so far as possible by the same technicians and usually at the same time of day, about 4:00 P.M. Determinations of hemoglobin were made colorimetrically, using a standard of 15.6 gm. per 100 c.c. of whole blood. When the blood of any of the workers showed abnormalities, counts were taken at more frequent intervals until the significance of the deviation could be determined. Elevated polymorphonuclear counts associated with acute respiratory disease were discounted as a possible response to radiation.

It is realized that more frequent counts might have been desirable from the scientific standpoint, but in view of the practical considerations of time consumed and the difficulty of assembling men actively engaged in diverse and often scattered work, a more frequent check seemed unnecessary except in special instances.

Although heavy irradiation over large fields can produce marked changes in the number of blood platelets (3), the hazard in the slight chronic exposures to which this group are subject does not seem to be of sufficient importance to warrant making actual platelet counts. So far as estimations from the smears were concerned, no one of the subjects showed any deviation from the normal. No significant morphologic abnormalities were found in examination of the smears. A few showed minor variations in red cells, as slight anisocytosis or polychromatophilia.

The Harvard cyclotron group has included 34 workers and the Technology group 51. There have been changes in personnel, but a number have continued from the first. Forty-two were followed over a year. Several of each group had only casual contact with the cyclotron or its products. A special effort was made with all the workers to maintain adequate dietary intakes with due regard to the amount of iron and vitamins available. If any tendency toward secondary anemia was noted, an effort was made so to supplement the diet as to insure an excess above normal requirements. Several workers not previously exposed to radiation showed high initial white counts, from 13,000 to 16,900 with no evident disease. These

were watched with special care. Three showed probably significant fluctuations in count, and two in whom these fluctuations recurred were advised to discontinue their work with radiation. The counts of the others either remained within normal limits or such variations as occurred could be explained by incidental factors, as respiratory infections, acute gastroenteritis, or bleeding from a peptic ulcer.

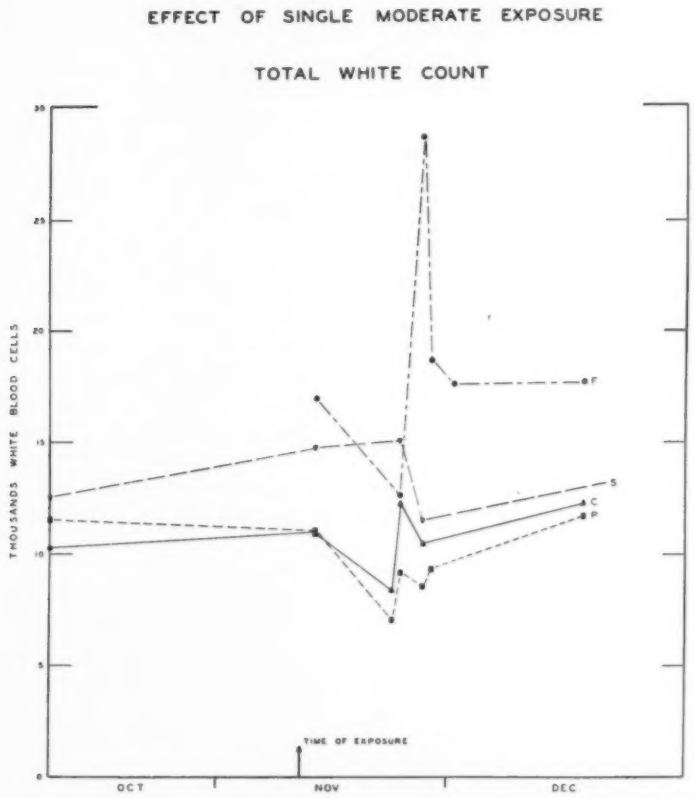


Fig. 1. Leukocytic response of four different workers receiving approximately the same amount of neutron radiation.

Of special interest is the fact that four workers received a moderate exposure when one of the cyclotrons was first operated. The amount of the exposure is not exactly known, but was probably in the order of 60 r distributed over the body. As would be expected, these workers showed an initial drop in total white cell count. The changes noted in the circulating cells are presented in Figure 1. The fall was more marked in the lymphocytes than in the polymorphonuclear leukocytes. This was followed promptly by a compensatory rise which, in the case of F (Fig. 2), who normally ran a high white count (one taken routinely in 1936 was 13,550 and one in 1939 was 15,400), reached a total of over 28,000. The white count returned in a week to levels only slightly above those previously carried. In the other workers only minor variations occurred in white cell count at first. During subsequent months F's white count rose somewhat, ranging between 16,000 and 22,000 until a year after the initial exposure, when a second exposure

rather greater than usual, but of unknown amount, occurred. Later a compensatory rise in the total white count to 31,000 occurred. At this time the differential count was: polymorphonuclear leukocytes 55 per cent, lymphocytes 37 per cent, large mononuclear leukocytes 5 per cent, eosinophils 1 per cent, immature mononuclear leukocytes 2 per cent. Platelets were normal. The red cell count was 5,500,000 with 86 per cent hemoglobin. A smear showed a moderate degree of achromia with slight anisocytosis and occasional polychromatophilic red cells. A few polymorphonuclear leukocytes showed toxic granulations. At this time his work with the cyclotron was stopped and in the next five months the white cell count gradually dropped to 19,300. The red cell count remained elevated to 5,410,000 but with some secondary anemia and a hemoglobin of 78 per cent. Fourteen months later the white cell count was 16,500, the red cell count 5,640,000, and the hemoglobin 90 per cent (14 gm.).

In contrast to this was case C (Fig. 3), which showed relatively little response following the initial exposure but a gradual increase to a count of 15,400 in the next two months; this was followed by a gradual drop. During the summer vacation the white cell count fell to 10,000, where it remained during the fall. A year and two months after the initial exposure the white count began to climb again, remaining for several months in the neighborhood of 16,000. During this time an acute respiratory infection brought the total white count up to 19,000. At the end of this period associated with rest from radiation, the white cell count fell, fluctuating between 8,900 and 12,100. Two and a half years after the initial exposure the white cell count was 14,350, with 70 per cent polymorphonuclear leukocytes, 5 per cent eosinophilic leukocytes, 1 per cent basophils, 16 per cent lymphocytes, 6 per cent large mononuclear leukocytes, 1 per cent large lymphocytes, and 1 per cent immature white cells. This person is planning to discontinue work with the cyclotron.

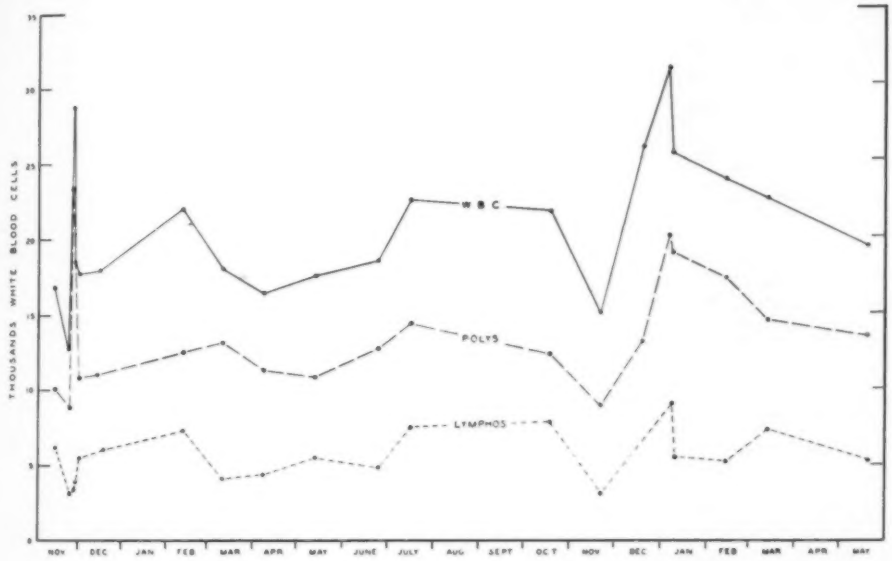
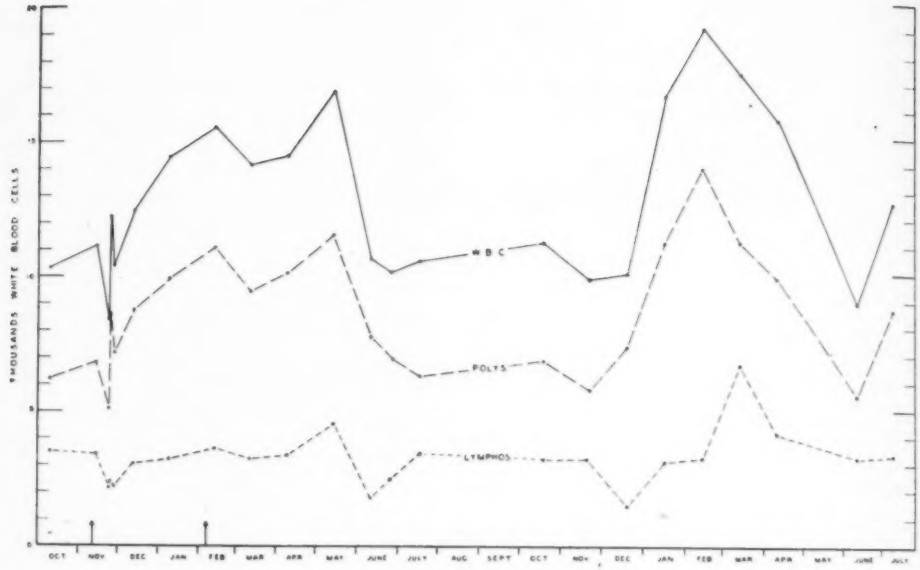
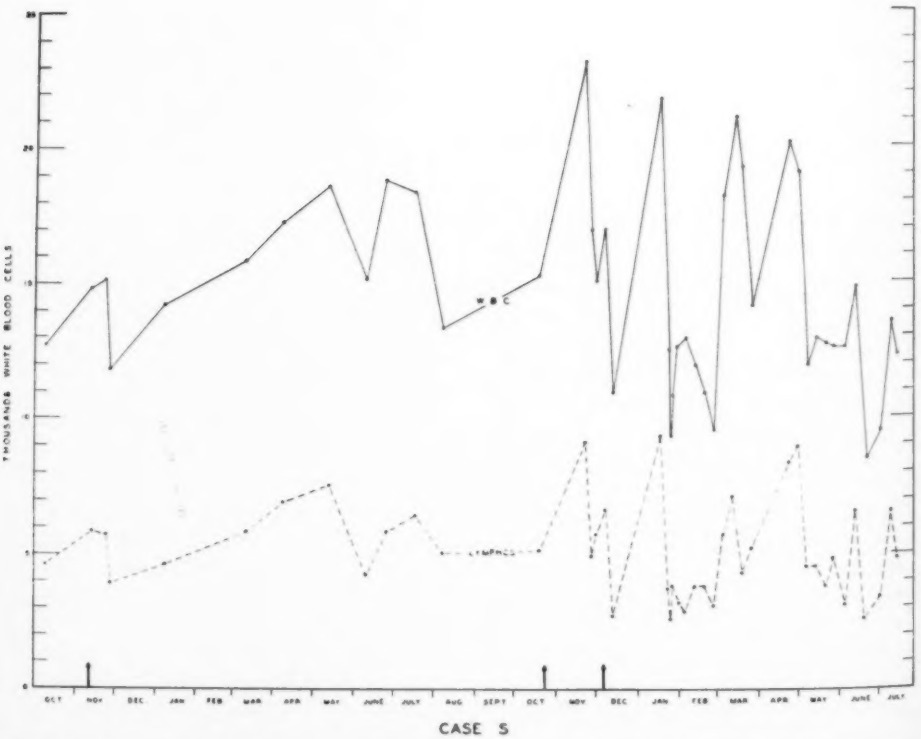


Fig. 2. Case F.: Note response shown in Fig. 1 and subsequent course indicating unstable hematopoietic mechanism.



CASE C



CASE S

Figs. 3 and 4. Cases C and S. In case C the fluctuations are of lesser order than in case F (Fig. 2). Case S is characterized by marked fluctuations in leukocytic count and relative elevation of lymphocytes.

Case S (Fig. 4) is one of the most interesting because of the variable character of the white cell count, suggesting an easily affected or unstable bone marrow. The marked fluctuations in total white cell and in lymphocyte counts are very clearly shown in the figure. It is not certain that the fluctuations shown in the last six months of the graph are due to radiation, but the assumption is that such is the case. This person was warned soon after the unstable character of his white cell count became apparent to discontinue work with radiation (chiefly gamma radiation from radioactive carbon), but he was unwilling to do so until the last few months shown in the graph. His final white cell count, at the end of twenty-one months under observation, was 12,300. The platelets were normal. The red cell count was 5,530,000, hemoglobin 110 per cent. The differential count showed polymorphonuclear leukocytes 59 per cent, eosinophils 4 per cent, lymphocytes 26 per cent, large mononuclear leukocytes 10 per cent, atypical lymphocytes 1 per cent. Previously the smear had shown a scattering of metamyelocytes and young lymphocytes. We regard the response shown in this instance as one which should not be permitted to occur. Incidentally, had this person had counts done only once in two or three months, many of the fluctuations would have been missed.

In the Massachusetts Institute of Technology group, consisting of 51 persons whose periods of exposure ranged from thirty to three months, the majority well over a year, no significant fluctuations were encountered. One of the workers, then in another laboratory, had about a year previously discontinued work in radiation for some months as a result of a mild secondary anemia attributed to exposure to neutrons. He has shown no hematologic abnormalities since.

Red cell counts above 5,000,000 and hemoglobin levels above 100 per cent were of not infrequent occurrence, although not constant findings. Thus, in one individual with 22 determinations from October 1939 to March 1942, 18 gave counts above 5,000,000, the high point being 5,558,000, and 14 showed a hemoglobin above 100 per cent. No changes referable to radiation were encountered. The lowest red cell count and hemoglobin were associated with an acute respiratory infection. None of the group developed a persistent anemia. In no smears were nucleated red cells found.

SUMMARY AND CONCLUSIONS

1. The blood counts and hemoglobin levels of 85 persons more or less exposed to slight radiation from cyclotrons and temporarily radioactive isotopes have been followed for periods varying from three to thirty months.

2. Most persons under these conditions show no significant changes that are not explained by intercurrent disease.

3. Four showed minor variations in white cell count.

4. As with exposure to x-ray or radium radiation, transient depression in white cell count is followed by elevation. This change occurs more rapidly in lymphocytes than granulocytes.

5. Some persons have an unstable bone marrow as shown by marked fluctuations in white cell counts when subjected to only minor exposure to radiation. Such persons should not work where they are exposed to radiation.

6. The precautions for the safety of these two groups of cyclotron workers appear adequate.

I am indebted to Dr. Herman Lisco for aid in some of the examinations.

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Pyloric Ulcers[1]

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THERE OCCUR in the pyloric valve a few peptic ulcers showing certain characteristics which differentiate them from both duodenal and prepyloric ulcers. The separation of these pyloric lesions from the prepyloric group is of special importance because of the high incidence of malignancy in the latter. In a series of 128 proved benign gastric ulcers reported by Holmes and Hampton (1) in 1932, 28 were classified as pyloric. Doub (2), of the Henry Ford Hospital, Detroit, reported 10 pyloric ulcers, of which two were proved malignant. Butsch (3), of the Mayo Clinic, reported 46 cases of ulcer actually located in the pyloric sphincter. Thirty-five of these were localized at operation but the diagnosis could not be further confirmed, since resection was impossible, due to the severe inflammatory reaction present. Ten were resected and all proved to be benign. Some of them may have invaded the pylorus by extension from either side, for the authors felt that true pyloric origin was rare. Actual figures for the various locations were not given.

The controversy concerning ulcers in the vicinity of the pylorus which arose after the report from the Massachusetts General Hospital may be explained in large part on two separate grounds. First, the pathologists are not in accord as to what constitutes malignancy. In the second place, the criteria specified in that report have not been strictly followed. According to the authors' original premise, "any chronic, indurated, ulcerating lesion occurring in the pyloric antrum within 1 inch of the pylorus, but not involving the pylorus, should be considered malignant until proved otherwise"; also, pyloric ulcers extending into the stomach are not classified as prepyloric. A review of the recent literature on the subject seems to show that there is some digression from this definition, which may account in part for the discrepancies in the ratio of benign to malignant lesions in this part of the stomach. Whether one accepts the high ratio of malignancy reported by Holmes and Hampton (12 to 1) or the almost opposite ratio of other authors, all agree that the chronic or recurring ulcerating prepyloric lesion should be resected. It should be noted that this specifically excludes not only the acute gastric ulcer that heals promptly and does not recur, whatever its location, but the pyloric ulcer as well. I believe that many pyloric ulcers, and even some ulcers located in the base of the duodenal cap, are erroneously classified as prepyloric by radiologists, and so fall into the group of probable malignant neoplasms.

Horsley (4), in 1936, reported 12 cases of pyloric ulcer which were verified as to location by pathologic examination after partial gastrectomy. Taking them as a group, he made the following observations: They represented 7 per cent of a total of 173 gastric resections for peptic ulcer. Because of their location, spasm out of proportion to the size of the lesion was seen by x-ray examination; twenty-four-hour retention was also demonstrable. Six of the series were said to be typical ulcers, but these are not described nor are illustrations shown. The average age of the patients was 46.6 years; 10 were men and 2 were women. The average duration of symptoms was ten years and nine months, with recent development of acute symptoms. The average hydrochloric acid content of the gastric juice was 32.9 per cent, the highest figure being 75 per cent. In the series reported from the Mayo Clinic, referred to previously, the average age of

[1] Read before the New England Roentgen Ray Society, Boston, Nov. 15, 1940. Accepted for publication in March 1942.

Fig. 1. Typical duodenal ulcer defect.
Fig. 2. Ulcer in the base of the duodenal cap. For details of this and other cases illustrated, see text.

the patients was forty-seven years, with 41 males and 5 females. The average duration of symptoms was six and a half years, with frequent episodes of obstruction. The average hydrochloric acid content of the gastric juice was 36.5 per cent, or 6.7 per cent below the group average for gastric ulcer; 11 per cent showed achlorhydria. The lesion was localized by roentgenologic examination in only 4 cases. In 18 cases it was described as being near the outlet of the stomach; in others it was called simply gastric or duodenal ulcer.

The present report concerns 10 cases of acute pyloric ulcer. Several were seen which showed similar deformity but without demonstration of a crater; these are not included. Of the 10 cases, the location of 2 was confirmed by pathologic examination of the resected specimen, and 3 were localized at operation. All showed certain similar and distinctive characteristics on the x-ray film. Seven of the 10 patients were men and 3 were women. The ages of the patients varied from thirty-seven to sixty-five years. The duration of symptoms ranged from one week to twenty years. Two cases showed obstruction. The hydrochloric acid content of the gastric juice varied from 24 per cent to 70 per cent.

The object of this report is to present and illustrate pyloric ulcers as a distinct and recognizable entity. The following brief case reports with accompanying illustrations are given in an attempt to reproduce a picture of that entity.

For proper orientation, Figure 1 shows a typical duodenal ulcer defect, with a normal stomach outline, a well differentiated sphincter, and distention of the smooth base of the duodenal cap. Figure 2*a* shows an ulcer which lies in the base of the cap. The sphincter is well differentiated when the antrum is filled out, as shown in Figure 2*b*. It seems to me to be important to have a good roentgenogram of the entire stomach and duodenum on one film, in order to understand the exact relationships. This patient was operated on because of continued pain and partial obstruction. Because of the marked inflammatory reaction in the region of the ulcer it was not resected and a posterior gastro-enterostomy was done. The ulcer was localized to the duodenum.

Figure 3*a* shows a lesion similar both as to localization and appearance, but unconfirmed otherwise. Figure 3*b* shows the relationship of antrum and sphincter to the base of the cap. Figure 4 shows a somewhat similar duodenal ulcer which is closer to the sphincter. It should be noted that in all these cases, even though the ulcer crater is next to the sphincter, there is no distortion of the sphincter.

Figure 5*a* shows marked narrowing and irregularity of the base of the cap and the

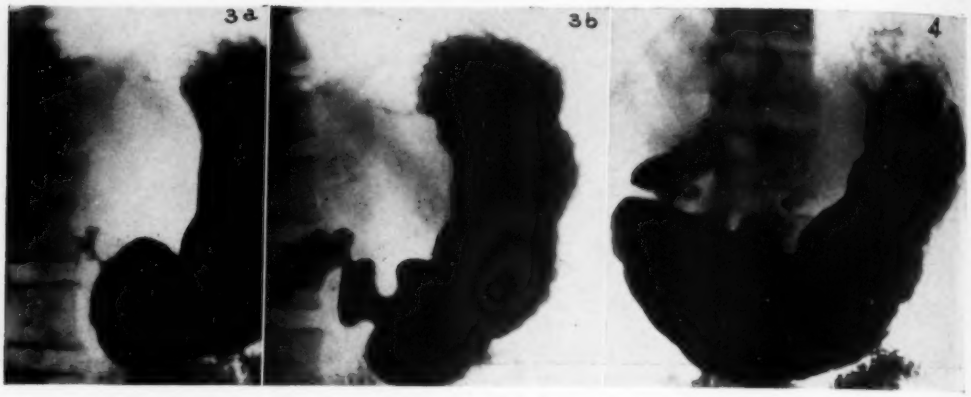


Fig. 3. Ulcer similar in appearance and location to that shown in Fig. 2.
Fig. 4. Duodenal ulcer closer to the sphincter than that shown in Fig. 3.

sphincter. The prepyloric area is narrow but flexible, as compared with that shown in Figure 5*b*. The ulcer crater is similar to those in the previous illustrations but has also a somewhat collar-button appearance. This patient was operated on because of continued pain, vomiting, and obstruction. The operative report states that there was a stenosing ulcer at the pylorus on the duodenal side. The stomach was dilated and its wall thickened. Because of the patient's general condition, a posterior gastro-enterostomy was done.

Figure 6*a* shows the first of the pyloric group in which resection was performed. The patient was fifty-six years old. He had had a cholecystectomy in 1924, following which he had been symptom-free until his present illness. One week before admission, he had several teeth extracted from the upper jaw. Two days later, that is five days before admission, he began to have severe epigastric pain and vomited material resembling coffee grounds. The day of admission he had one tarry stool. Figure 6*a* shows an ulcer which seems to be some distance from the partially filled cap. It has the collar-button appearance of the ulcer shown in Figure 5*b*. Figure 6*b*, in which there is better filling of the antrum, shows how close the ulcer really is to the base of the cap. The cap is definitely defective on the lesser side. Ten days later (Fig. 7*a*), under medical treatment, the ulcer had decreased in size. It can be seen that, as it becomes smaller, the collar-button appearance is still present. The relationship of the ulcer to the base of the cap and the sphincter is much more obvious, and the crater seems to be closer to the cap. Figure 7*b*, with better filling of the antrum, shows that the crater is in the sphincter area. The base of the cap is still defective. Because of controversy as to the location and possible malignancy of the lesion, a resection was carried out. The operative report stated that the ulcer was in the sphincter. The pathologic report, by Shields Warren, reads: "The major portion of the mucosa was negative, but on the duodenal slope of the pyloric sphincter was a 5-mm. ulcer 4 mm. deep, with spoke-like rugae above it. Microscopic diagnosis: chronic peptic ulcer."[2]

The next case illustrated is that of a thirty-seven-year-old man who had had indigestion more or less constantly for six years. In Figure 8*a* may be seen the appearance of the ulcer in October 1938. The picture resembles that shown in Figure 7*b*. The collar-button effect is not so obvious, but the ulcer is situated on the lesser side in an area of narrowing which seems to be at the expense of both cap and prepyloric areas. It was originally labeled a duodenal ulcer. Three and one-half

[2] This case is reported by courtesy of Dr. Howard M. Clute.

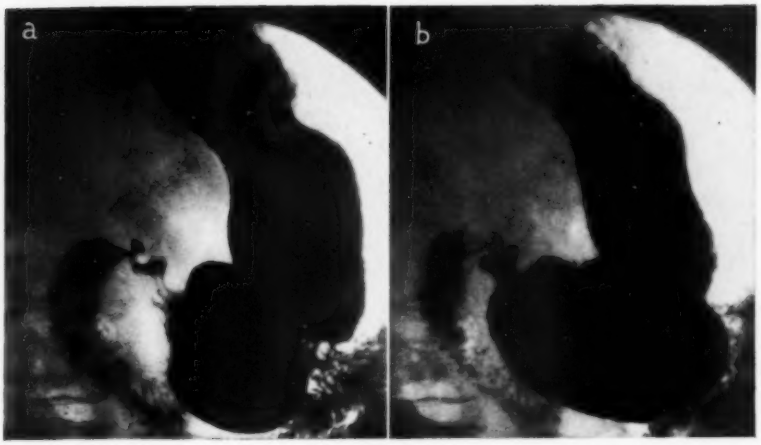
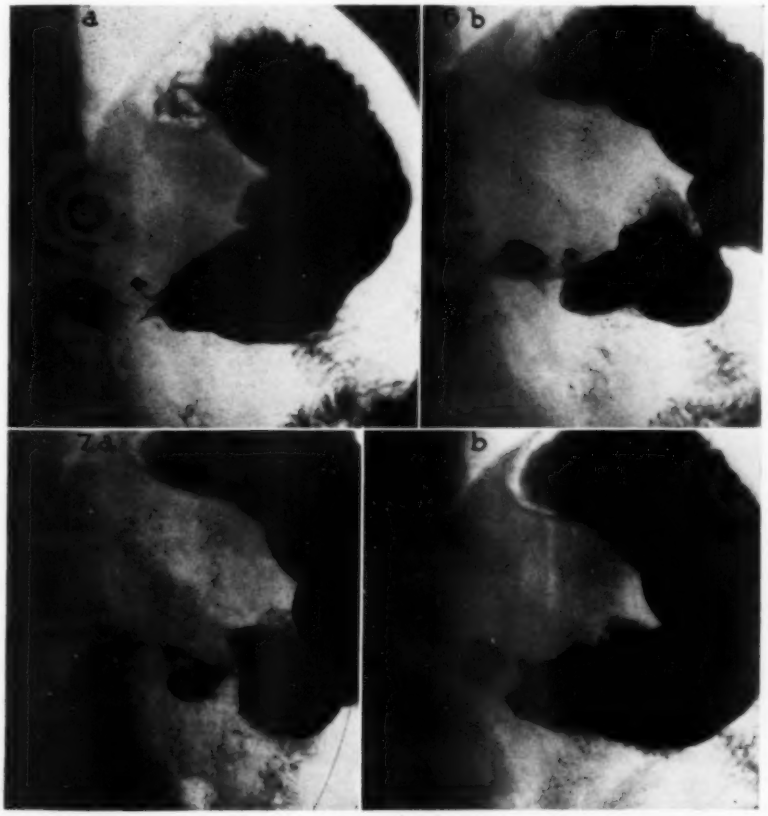


Fig. 5. Stenosing ulcer at the pylorus, on the duodenal side.



Figs. 6 and 7. Ulcer in the pyloric sphincter before and after medical treatment.

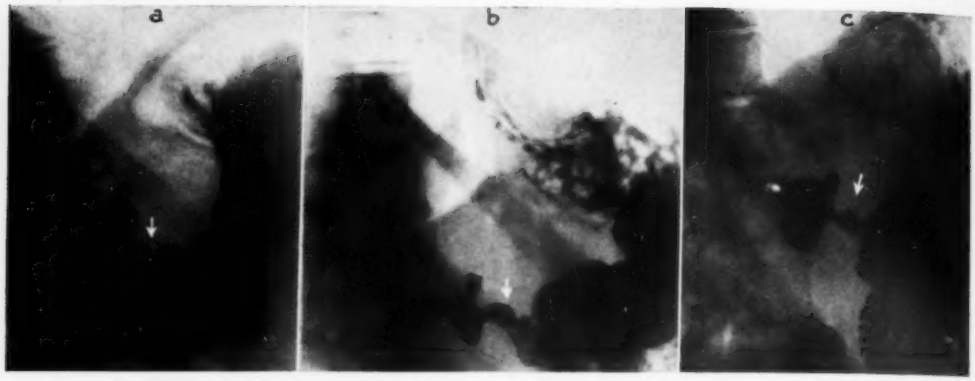


Fig. 8. Ulcer of pyloric sphincter, extending onto the duodenal side.

months later (Fig. 8*b*) the crater was much larger, but the duodenal deformity was also larger. The collar-button effect was more noticeable. After two weeks of strict bed rest and ulcer régime, there was a definite diminution in the size of the crater (Fig. 8*c*), and the duodenal and antral deformities were less marked. Since the location was not definitely determined, an exploratory operation was performed. The operator could not tell on which side of the sphincter the ulcer lay, so that a partial gastric resection was done. The report of J. B. Hazard, the pathologist, reads: "Including the major portion of the sphincter in width, and extending onto the duodenal side, is an ulceration on the lesser side. Half is absent due to adherence to the pancreas. Microscopic diagnosis is benign peptic ulcer."[3]

In Figure 9*a* may be seen a small ulcer crater on the lesser side of a very wide sphincter, with some deformity of the prepyloric region and marked deformity of the base of the duodenum. The patient was a forty-four-year-old physician who had had epigastric distress and anorexia for two months. He also had gallstones. Although the patient's condition improved on medical treatment (Fig. 9*b*), the location was thought to be prepyloric and an exploratory operation was carried out. The operative report states that in the pylorus there was the scar of a healed ulcer which had involved both prepyloric and duodenal aspects, but especially the duodenum. A cholecystectomy was done. Roentgenograms were made a year after this and no change in the appearance of the stomach and duodenum was seen. At present, five years later, the patient is alive and well.

The next case is that of another physician, aged fifty-seven years, who had had what he called ulcer pain for twenty years. This pain had stopped two years before entry when he had stopped drinking coffee. Two months before entry, he began to have epigastric pain and for three days had tarry stools. Pain continued until entry, but was relieved by food and alkali. In Figure 10*a* may be seen the characteristic deformity of the previous ulcers, with a small collar-button crater on the lesser side of a tremendously broad sphincter. The deformity involves the lesser side of both the base of the cap and the prepyloric area. One week later (Fig. 10*b*) the cap had relaxed and the actual penetrating lesion had disappeared. There was left a small fleck on the lesser side of the sphincter with equal amounts of deformity on either side. One week after Figure 10*b* was taken the entire area had become smooth, but the broad sphincter still remained (Fig. 11*a*). No symptoms were present at this time. The stomach emptied rapidly on all occasions. The patient has returned to the

[3] This case is reported by courtesy of Drs. Stanley Kimball and Marshall K. Bartlett.

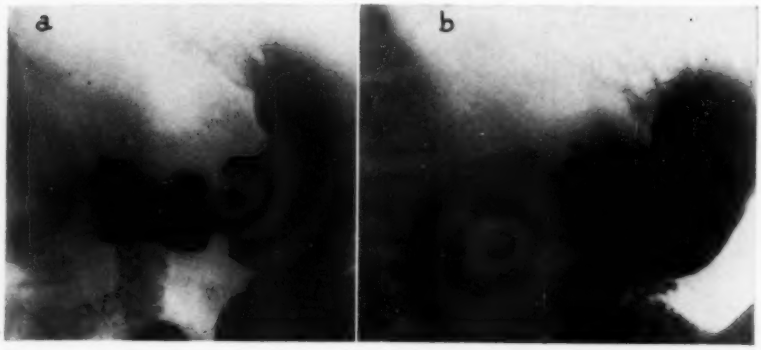
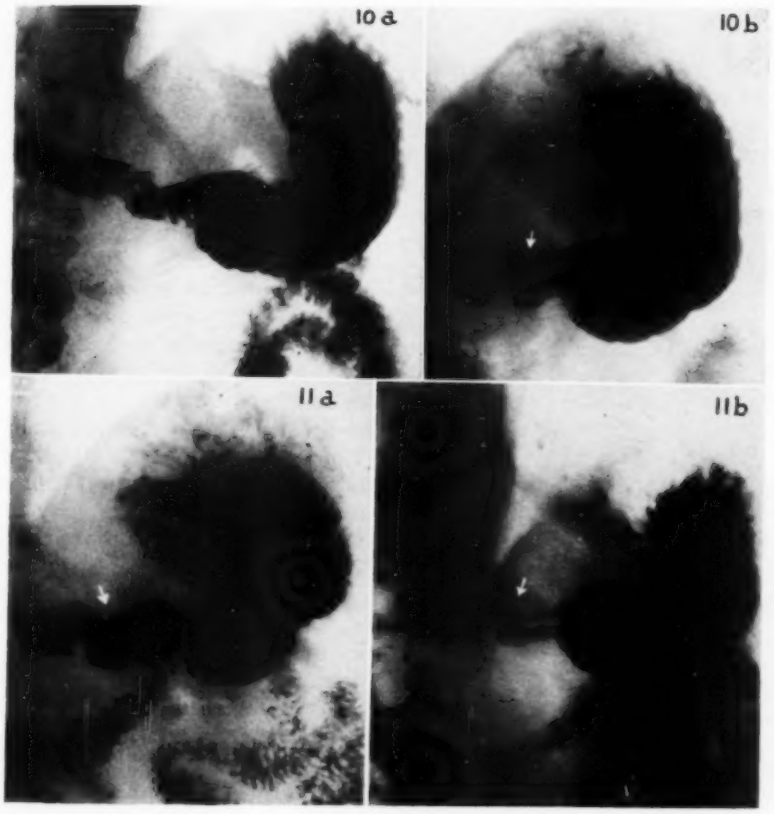


Fig. 9. Small ulcer crater on lesser side of a wide sphincter.



Figs. 10 and 11. Recurrent ulcer, involving lesser side of both the base of the duodenal cap and the prepyloric area.

clinic at regular intervals and has continued to be symptom-free, though it is now four years since he was first seen. Roentgenograms taken after three years showed no change in appearance (Fig. 11*b*).

The case shown in Figure 12*a* was not

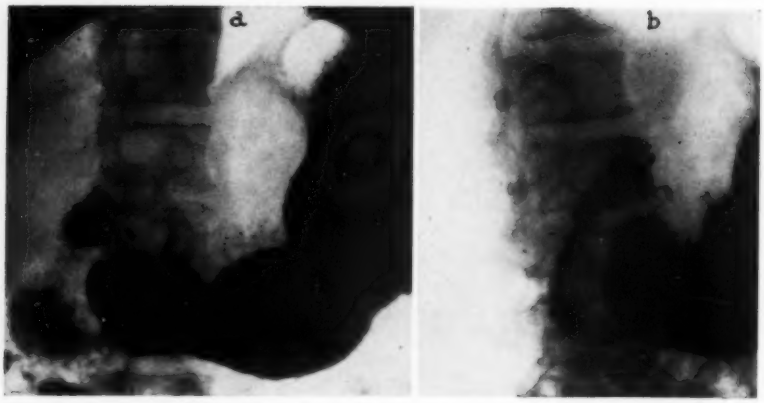


Fig. 12. Ulcer of the pyloric sphincter, probably involving base of duodenal cap (unverified).

verified in any other way, but the lesion is so similar in appearance to the others that I am sure it was in the sphincter and probably involved the base of the cap. The coarseness of the rugae in the duodenum and the spasm or induration in the prepyloric area are nicely shown in Figure 12*b*.

Fig. 13. Typical prepyloric ulcer.

In order to show an ulcer that is typically prepyloric in location, Figure 13 is presented. The patient was a twenty-two-year-old nurse, who had had upper abdominal distress for approximately one month. Note that the duodenal cap, its base, and the sphincter are all clearly differentiated, and the ulcer crater is definitely on the stomach side of the sphincter. Roentgen evidence of the lesion disappeared and symptoms ceased in two weeks.

I do not wish to leave the impression that the localization of prepyloric ulcers is always as easy as in this last instance, but I firmly believe that many cases in which the location is obscured by spasm and inflammatory changes are more easily localized after a period of medical treatment. I also believe that the appearance of the base of the cap is all important in the localization of the ulcer. By that I mean that if there is deformity of the base of the cap, together with a poorly differentiated sphincter and prepyloric area, subsequent examination will show that the ulcer was in the sphincter or duodenal slope of the sphincter. This localization can be demonstrated if weekly check-up roentgenograms are made during the healing period.

Despite the fact that some of the pyloric ulcers are reported as malignant, the evidence obtained from the literature is that most are benign lesions. I do not believe that the majority of these patients should be subjected to a resection of the stomach on the chance of discovering early malignant change in a relatively small percentage of cases.

SUMMARY

Ten cases of active pyloric ulcer are reported. In several cases not included in this number deformities similar to the healed deformities of this group were observed, which probably represent healed pyloric ulcers. Of the 10 active ulcers, 2 were localized and proved benign by histologic section; in 3 patients the lesion was localized at operation, and of these, 1 is well five years later and 2 are well three years later. In 5 cases the ulcers were localized only by roentgen examination. One of this group is well five years later, 1 has been well three years, 2 are recent cases, and the fifth patient died of another disease a few months later. The series thus tends to substantiate the claim of others that pyloric ulcers are benign.

Roentgenographically, the characteristics of these ulcers are: deformity of both the prepyloric area and the base of the cap; distortion and broadening of the pyloric sphincter, especially as healing occurs; a penetrating type of ulcer crater, usually on the lesser side of the sphincter.

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Incidence of Multiple Primary Tumors and the Problem of Acquired Cancer Immunity[1]

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WHILE MULTIPLE tumors of *identical* type are frequently encountered in the same person, as for instance in all cases of multicentric skin lesions and of metastasis, we are justified in speaking of multiple *primary* tumors only when we are reasonably sure that such tumors have developed independently and have no ascertainable direct or indirect connection with each other.

This lack of connection is obvious in the case of combinations of tumor types entirely dissimilar morphologically and clinically, as for example tumors arising from embryologically different layers, as connective tissue and epithelium, and in the case of manifestly benign tumors and definitely malignant neoplasms. On the other hand, the differential diagnosis may become extremely difficult or even impossible if we are confronted with a combination of morphologically or clinically similar tumors.

To exclude metastases, Billroth formulated the following postulates, which he believed should be fulfilled before a diagnosis of multiple *primary* tumors can be given:

(1) That the tumors have a different anatomical structure.

(2) That each tumor be histogenetically derived from the tissues of the organ in which it is primarily found.

(3) That each malignant growth have its own metastases.

These requirements appear too strict. It is impossible to insist on metastasis as a diagnostic *sine qua non* in every case of malignant neoplasm. In addition, it is well possible that, because of a variety of factors, a tumor may be modified in structure and character to such a degree as almost completely to lose its original type and identity.

Etiologically, tumor multiplicity may be explained as the effect of multiple cell implantation, of multiple stimuli, or of multiple primordial cell nests (*Geschwulst-Anlagen*). Lubarsch interprets the occurrence of multiple tumors as evidence of a general tumor diathesis, while Walter thinks that in the majority of cases it signifies nothing more than a coincidence.

Among 3,700 consecutive autopsies performed by the Department of Pathology of the University of Colorado Medical School from 1925 to 1940, 42 examples of multiple primary tumors were recorded. An analysis of these cases shows that in 38 instances two tumors were found in the same person, while in 4 cases the patient harbored three tumors.

A combination of benign tumors only was seen but twice. The most frequent combination was that of a benign and a malignant tumor. This combination was seen in 27 patients. The combination of two benign tumors and one malignant tumor occurred in 3 cases. In 9 cases, two independent malignant tumors were observed simultaneously, while in still another case two primary malignant tumors were seen together with a benign tumor. Translating these numbers into percentages, we find that in approximately three-fourths of all cases of multiple tumors (76 per cent) a combination either of benign tumors or of malignant and benign tumor is present; in only about one-fourth of the cases (24 per cent) are *two malignant* tumors simultaneously observed. Considering the total of all autopsies, the percentage of multiple primary tumors amounted to 1.1 per cent; that of primary

[1] From the Department of Radiology of the University of Colorado School of Medicine and Hospitals, Denver, Colo. Presented before the Radiological Society of North America at the Twenty-seventh Annual Meeting, San Francisco, Calif., Dec 1–5, 1941.

TABLE I: MULTIPLE TUMORS: BENIGN + BENIGN AND MALIGNANT + BENIGN

Benign + Benign (2 Cases)
1. Adenoma, adrenals + Fibroadenoma, uterus
2. Mixed tumor, parotid + Osteoma, skull

Malignant + Benign (27 Cases)
1. Cancer, stomach + Fibroadenoma, breast
2. Cancer, stomach + Papilloma, rectum
3. Cancer, stomach + Papilloma, stomach
4. Cancer, stomach + Hemangioma, liver
5. Cancer, colon + Adenoma, pancreas
6. Cancer, colon + Adenoma, thyroid
7. Cancer, colon + Fibromyoma, uterus
8. Cancer, esophagus + Fibromyoma, uterus
9. Cancer, esophagus + Adenoma, liver
10. Cancer, small intestine + Adenoma, kidney
11. Cancer, small intestine + Adenoma, parathyroid
12. Cancer, bile duct + Fibromyoma, uterus
13. Cancer, liver + Fibroma, scrotum
14. Cancer, lung + Adenoma, adrenals
15. Cancer, bronchogenic + Neurinoma, acoustic nerve
16. Cancer, breast + Fibromyoma, uterus
17. Cancer, breast + Leiomyoma, uterus
18. Cancer, bladder + Fibroangioma, broad ligament
19. Cancer, prostate + Fibromas, rectum
20. Hypernephroma, kidney + Lymphangioma, small intestine
21. Sarcoma, thyroid + Adenoma, adrenals
22. Malignant melanoma, skin + Papilloma, skin
23. Medulloblastoma, brain + Papilloma, tube
24. Medulloblastoma, brain + Neurofibroma, jejunum
25. Spongioblastoma, brain + Fibromyoma, esophagus
26. Glioma, brain + Fibromyoma, uterus
27. Pinealoma, brain + Leiomyoma, uterus

Malignant + Benign + Benign (3 Cases)
1. Cancer, stomach + Fibroma, ovary + Fibrolipoma, kidney (Cancer metastasis in ovarian fibroma)
2. Cancer, ileum + Hemangioma, liver + Subcutaneous fibromas
3. Cancer, breast + Fibromyoma, uterus + Adenoma, kidney (Cancer metastasis in adenoma)

malignant tumors to about one-fourth of 1 per cent (0.27 per cent).

The two cases of multiple primary benign tumors occurred in a woman and a young man. In the woman, a fibromyoma of the uterus had been diagnosed clinically; in addition to this, autopsy showed adenomas of both adrenals. The young man had been treated both surgically and radiologically for mixed tumor of the parotid gland. This tumor had responded fairly well to therapy without ever disappearing completely. A few years later, a large osteoma of the frontal bone was observed, which failed to respond to any form of treatment. The patient later succumbed to a pneumonic infection.

TABLE II: MULTIPLE TUMORS: MALIGNANT + MALIGNANT AND MALIGNANT + MALIGNANT + BENIGN

Malignant + Malignant (9 Cases)
1. Adenocarcinoma, thyroid + Squamous-cell carcinoma, brain
2. Adenocarcinoma, kidney + Glioma, brain
3. Adenocarcinoma, sigmoid + Basal-cell carcinoma, chest wall
4. Adenocarcinoma, sigmoid + Adenocarcinoma, prostate
5. Adenocarcinoma, sigmoid + Cancer, bladder
6. Adenocarcinoma, sigmoid + Cancer, appendix
7. Adenocarcinoma, stomach + Bronchogenic carcinoma
8. Adenocarcinoma, stomach + Cancer, bladder
9. Adenocarcinoma, colon + Cancer, breast

Malignant + Malignant + Benign (1 Case)
1. Cancer, breast + meningioma, skull + leiomyoma, uterus

The combination of benign and malignant tumors offers little of interest either pathologically or clinically. The tumor types are so different that the diagnosis of independent multiplicity is easy. Among the benign tumors, fibromyomas of the uterus were the most prevalent; adenomas in various locations were next in order. The most frequent site of the malignant tumors was the gastro-intestinal tract (about 50 per cent of the cases), with brain tumors next. Most of the malignant growths were carcinomas; but one sarcoma was observed. The variety of tumor types and locations was so great as to preclude any conclusions as to etiology or interrelation (Table I). In two cases, however, an interesting phenomenon was seen, *i.e.*, metastasis from the malignant tumor to the benign tumor. In one instance an adenocarcinoma of the stomach had metastasized to a fibroma of the ovary. In the second case, an adenocarcinoma of the breast was observed simultaneously with a fibromyoma of the uterus and a benign adenoma of the kidney. Autopsy revealed cancer metastasis in the renal adenoma. According to Black and Gray of the University of Colorado, who surveyed these cases, only 22 examples (including ours) of metastasis from one tumor to another have been recorded in the literature.

The multiple malignant tumors present certain difficulties, especially with regard to differentiation from tumor metastases (Table II). In 4 cases, however, this dif-

ferentiation was comparatively simple: (1) an adenocarcinoma of the thyroid and squamous-cell cancer of the right parietal lobe of the brain; (2) an adenocarcinoma of the kidney and glioma of the brain; (3) an adenocarcinoma of the sigmoid and basal-cell carcinoma of the chest wall; (4) a carcinoma of the breast combined with a meningioma of the skull. In the remaining cases, we had to rely entirely on the opinion of the pathologist that the two simultaneously encountered tumors were so different in structure, type, and location as to exclude interrelation or metastasis. In this series, also, adenocarcinomas of the gastrointestinal tract were preponderant.

Our ratio of benign-malignant combination to malignant-malignant combination is about 3 to 1, *i.e.*, considerably higher than that reported in the earlier literature (6 to 1, by Egli in 1914; 25 to 1, by Puhr in 1927). The explanation of our higher ratio lies probably in the inclusion of brain tumors, previously less frequently diagnosed.

It is of interest to the radiologist that, of the total of 42 cases, 24 were observed roentgenologically. In the benign-malignant group, the malignant tumor or its metastases were recognized in 17 out of 19 cases. In one case, a medulloblastoma of the brain escaped discovery; in another case, a cancer of the ileum. Another carcinoma of the ileum and a small sarcoma of the thyroid were roentgenologically detected only by their respective metastases.

In the benign tumor group, only one case was referred to the X-Ray Department and diagnosed without difficulty: the case of mixed tumor of the parotid and osteoma of the skull.

Six of the 10 patients with multiple malignant tumors were examined roentgenologically. In two cases, the combination of two malignant tumors was recognized as such: (1) a cancer of the breast combined with cancer of the colon; (2) a cancer of the stomach combined with cancer of the urinary bladder. A case of cancer of the sigmoid associated with cancer of the appendix was diagnosed as cancer of the sigmoid only. The failure to diagnose multiple malignant tumors more often is probably due to the fact that the observation of one tumor seems to obviate the necessity of further and more detailed investigation by either clinician or roentgenologist.

Several patients with malignant tumor received radiotherapy, but no data are available which might suggest any unusual observations or point to any modification in tumor behavior or final results engendered by tumor multiplicity.

The relative rarity of multiple primary malignant tumors may be due to various causes. (1) One cause may be that, in the majority of cases, the span of life is definitely limited and no time remains, therefore, for the development of additional neoplasms. (2) Another cause may lie in our diagnostic limitations, both in the living patient and postmortem. It is quite plausible that the overwhelming manifestations of one tumor, especially in the presence of metastases, may obscure the existence of a second tumor or that such a tumor may be misdiagnosed as a metastasis, just as it happens that the most meticulous clinical and pathological examinations fail to detect the primary tumor in some cases of metastasis. (3) A third cause for the rarity of multiple malignant neoplasms may lie in the existence of a certain, as yet little defined and apparently unstable, tumor resistance or tumor immunity produced by the first tumor.

The problem of tumor resistance and immunity was very acute before the First World War but had, in the interim, been somewhat neglected by medical research and left to exploitation by charlatans and quacks. In this country, however, Kaplan and Goldfeder in 1938 revived interest in the question by their interesting article on serum therapy in cancer. I have been able to confirm Kaplan's findings in a large number of patients and shall report my results in a later publication. Quite recently, study of this problem received further impetus by Peller of Johns Hopkins and New York University. Basing his conclusions on animal experimentation and statistical

human material, Peller claims immunization against visceral cancer by artificial production of practically innocuous and easily curable skin cancer. While it is too early to pass final judgment on Peller's work, which has been widely publicized by the daily press and news magazines but which has been challenged by other investigators, it must, nevertheless, be emphasized that research work in animals proves that such an immunization lies well within the realm of possibilities. The fact that Virchow smothered the idea with the weight of his authority, about sixty or seventy years ago, is no proof to the contrary; Virchow was brilliantly wrong in many things, as for example in his condemnation of Koch and the tubercle bacillus.

In animal experimentation, both a natural resistance to tumor invasion and an acquired tumor immunity can be distinguished. Malignant tumors transplanted from mouse to mouse fail to "take," at first, in a high percentage of cases. Only after adaptation does the percentage of positive "takes" increase, but even under the most favorable experimental circumstances a certain number of mice will remain permanently refractory to tumor implantation. On the other hand, if a mouse spontaneously overcomes tumor growth, or if a tumor is completely extirpated, the animal acquires a definite immunity, and further inoculations with the same tumor will be unsuccessful. Such an animal may even be immune to other types of tumor, a condition which differs from the more specific immunity in infection and has therefore been termed "pan-immunity" by Ehrlich. This immunity may even be conferred by inoculation of blood or tissue from another animal of the same species, but it is, in all cases, dependent on the transfer of *living* cells. To explain this immunity Ehrlich advanced his "athrepsia" theory, which presumed that tumor growth depends on the presence of specific nutritive substances. While this theory has been disputed by other investigators, the fact of tumor immunity in animals, natural or acquired, is now generally recognized.

We do not know yet to what extent, if any, these principles of immunity apply in human tumors. The question is obscured not only by the complete absence of experimental data in man but also by innumerable other factors involved in oncology, as heredity, sex, age, endocrine dyscrasia, malformation, irritation, trauma, infection, etc. The fact that none of the many tumor theories has proved applicable or satisfactory in all cases serves to illustrate the still prevalent confusion and uncertainty, and the possibility exists that future research may change or even destroy most of our cherished conceptions of classification. The flux in these matters is demonstrated by the sporadic appearance of entirely new and spectacular theories. I may call attention, for example, to the furore recently created in Europe by Kögl's theory of partial protein racemization. Even the apparently simple question of serologic reactions in tumor diagnosis is far from being settled.

It seems probable that elements of immunity and tumor resistance play a part in man and that there are processes at work similar to those described in animals. Spontaneous cures of neoplasms of undoubted malignancy have been reported occasionally, and all of us have been impressed by the unpredictably different course in certain apparently analogous cases. Whose prognostic ability has not been put to shame by the surprising longevity of some cancer patient given up as hopeless years previously? In my experiments with many adjuvants to the customary radiotherapeutic procedures, my skepticism has more than once been rudely shaken by unexpected improvements in radioresistant cases. Is the effect obtained by Kaplan's serum due only to an unspecific foreign-protein reaction, such as many cancer therapists have described after use of typhoid serum or diphtheria antitoxin, or is it specific in certain forms of malignant growth? Does the fact that in not a single case of our series a visceral malignant lesion was combined with skin epithelioma support Peller's contention, or is

this only incidental? Evidently it is too much to expect a definite specific action from one preparation in all cancer cases, since what we call "cancer" or designate as "malignancy" at the present stage of our knowledge may well be found in the future to be an ill-assorted conglomeration of pathological and clinical entities entirely different etiologically.

I am fully aware that I am venturing on dangerous ground in trying to discuss this subject, but my excuse is that any approach is justified to a problem which so far has largely eluded our best efforts and offers no promise of final solution by the methods conventionally employed. All of us have heard the accusation that the attitude of the radiotherapist and surgeon in cancer therapy is too narrow because both expect to cure by purely local procedures a pathologic process which, at the time of clinical diagnosis, has ceased in most cases to be a local lesion and has become a systemic disease. The same critics assert that success or failure consequently should not be gauged by statistical laurels in localized superficial lesions (which future pathologists may even refuse to classify as cancer) but by the results in visceral lesions. This skepticism and negativism have forced radiotherapy into a defensive position even where, just a few years ago, it seemed strongly entrenched, as in preoperative and postoperative irradiation of cancer of the breast. Though this skepticism is exaggerated and this criticism often unjust, they illustrate one fact, namely that, despite all our advances in technic and armamentarium, our final results fail to be satisfactory and unequivocal. There is no disagreement or criticism about the use or the value of insulin in diabetes or of salvarsan in syphilis.

And who is better qualified to blaze a trail in these matters than the radiologist? Personally I am convinced that he is not only able and broadminded enough but, in spite of all criticism, willing to carry the torch of research in the field of oncotherapy even if his investigation may—as is unavoidable—occasionally lead him beyond the restricted confines of kilovolts, roentgens, and specialty.

In conclusion, I wish to reiterate my opinion that the rarity of multiple primary tumors of malignant character may well be explained by factors of acquired immunity and that this may, in some future time, play an important part in our combat against tumor and malignant growth.

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DISCUSSION

Davis Spangler, M.D. (Dallas, Texas): This is a thought-provoking paper both in what it says and what it implies. The study of multiple tumors, so far as I am concerned, represents a new statistical grouping. That healing of a malignant tumor will tend to confer immunity to the development of other malignant growths within the body of a patient is a comforting theory, which, as Doctor Schmidt says, is far from proved. If we accept, even in part, the research, apparently confirmed, showing cancerogenic powers of modified estrogens, then we must expect that following the presence and/or disappearance of a single malignant tumor, this cancerogenic power has been lost or neutralized. From clinical experience I doubt the validity of this assumption. I have seen a patient with an arrested or healed giant-cell tumor die from a subsequent myelogenous leukemia, and another patient with carcinoma of the colon some years after healing of an epidermoid carcinoma on the hand.

I did not realize that multiple tumors were of such rarity, especially the combination of benign and malignant. Two leading pathologists of Dallas had the same reaction when I discussed this with them, though, like myself, they had not made any statistical study. Two cases which have come to my attention may be briefly reported:

1. A girl of fifteen, a patient of Doctor H. M. Doolittle, had a malignant melanoma removed from her back one year before we saw her. Examination showed a tumor of the left breast, which proved on amputation to be a grade III duct-cell adenocarcinoma. There were some lumps in her right breast at this time. Six weeks later a similar tumor had appeared in the right breast, proved by biopsy. This patient fell into the hands of a cancer quack and was dead in eight months.

2. The recent case of a negro woman, reported through the courtesy of Doctor Cochran, is also of interest. She showed at operation a mixed tumor of the parotid, an adenofibroma of the breast, and a rhabdomyosarcoma of the left rectus muscle sheath. Four months later another adenofibroma was removed from the breast. She is still alive.

In my limited experience the combination of a benign and a malignant tumor has not been infrequent, but the benign growth has been disregarded for the more important malignant tumor.

Henry J. Ullmann, M.D. (Santa Barbara, Calif.): I was much surprised at Dr. Schmidt's report of the statistical rarity of multiple cancer. I was of the impression, from my clinical experience, that these multiple growths are not uncommon. We have had one patient who was operated on for cancer of the bowel, in whom there was found a cancer of the ovary at the same time, which had been producing no symptoms. Another patient was referred to me with carcinoma of the cervix and at examination a cancer of the breast was also found. The cancer of the cervix was cured, as shown at autopsy six years later. Death was due to the breast cancer, despite radical mastectomy followed by postoperative irradiation. In still another case a basal-cell cancer of the skin with a squamous-cell cancer of the lip and a Bowen's cancer of the hand were seen in the same patient.

My experience has been that having one cancer does not confer immunity to another. I had a patient with a tumor of the breast, which was apparently cured, and she died later with cancer of the stomach. In another patient, with cancer of the prostate, cancer of the skin developed, and still another, who was cured of cancer of the skin, died of a cancer of the tonsil.

In so far as the simultaneous occurrence of benign and malignant tumors is concerned, fibroids and carcinoma of the cervix or corpus are so commonly found together, at least in my experience, that I am much surprised to hear that this combination is so rare.

Doctor Schmidt (*closing*): There is little which I can add to the excellent discussion by Dr. Spangler and Dr. Ullmann. I, too, was of the impression that multiple tumors are much more frequent than reports in the medical literature indicate. Possibly the coincidence is often not considered worth reporting. I think, however, that at least all cases of simultaneous multiple *malignant* tumors should be recorded. We all agree that, at the present time, nobody knows to what degree factors of immunity are involved. There are so many different types of tumor that we are not allowed to generalize. Personally I was interested to learn that practically everybody has observed multiple primary tumors. The news item about cancer experiments to which I referred, and which probably most of you have seen, was rather spectacular and might lead to the impression that from now on all one has to do is to get an artificial skin cancer, no matter by what means—by x-ray or any other way—to insure immunity against the more serious forms of visceral cancer. In other words: you just go and get your "cancer vaccination." As we all realize, this is nothing more than wishful thinking.

Argentaffin Tumors of the Small Bowel: A Roentgen Sign of Malignant Change[1]

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CARCINOIDS OR argentaffinomas are rare tumors originating in the argentaffin cells situated at the bases of the crypts of Lieberkühn in the gastro-intestinal tract. They are usually benign and of no clinical significance. We have, however, encountered three cases of malignant small bowel carcinoids, one at the New Haven Hospital and two at the University of California Hospital. Since no instance of a preoperative diagnosis of such tumors has been found in the literature, and since the diagnosis in our second case was made before operation, on the basis of the postoperative findings in the first case, we believe we have recognized a roentgen sign indicative of the presence of these neoplasms.

In the typical case, the patient is a middle-aged man or woman, who complains of long-standing gaseous distention, bloating, periumbilical pain, and steadily increasing loss of weight. Occasionally he has diarrhea and he may have "rumbling" or "rushes" in the abdomen. The clinical picture is one of chronic and increasing partial obstruction of the small bowel. The distention is usually so great that no tumor is palpable. The guaiac test for blood in the stool is usually negative since the tumors do not ulcerate or bleed.

Roentgenologically the small bowel is seen to be distended with gas and fluid up to a point of partial obstruction. On careful examination at the site of obstruction, a small filling defect can be found and the bowel is seen to be kinked. Since the primary lesion is usually small, the obstruction is due to knuckling of the bowel and not to the tumor. *It is the coexistence of kinking and tumor of the bowel which suggests the diagnosis.* Other small-bowel tumors, such as polyps, lipoma, and carcinoma, produce obstruction because of intraluminary growth of the lesion or intussusception of the bowel.

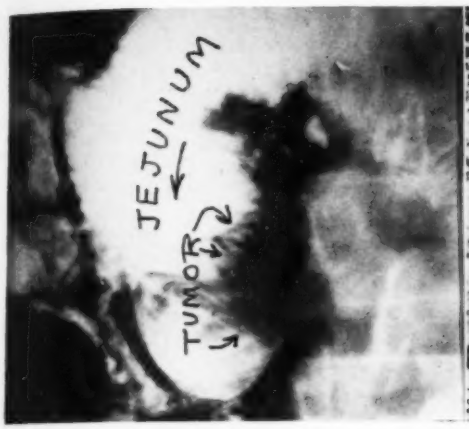
In the first case to be reported here the diagnosis was made postoperatively. In the second case, the diagnosis was considered as tenable because of the symptomatology and the presence of tumor at a point of kinking of the jejunum. These two cases present a fairly typical syndrome. A number of similar cases are described in the literature. The third case is of interest in that the first lesion recognized was in the rectosigmoid and proved to be a metastasis from a malignant carcinoid primary in the ileum. It emphasizes the nature of the spread of these metastases through the wall of the bowel with little encroachment upon the lumen. The constricting infiltration of the wall of the bowel and the mesentery causes varying degrees of obstruction.

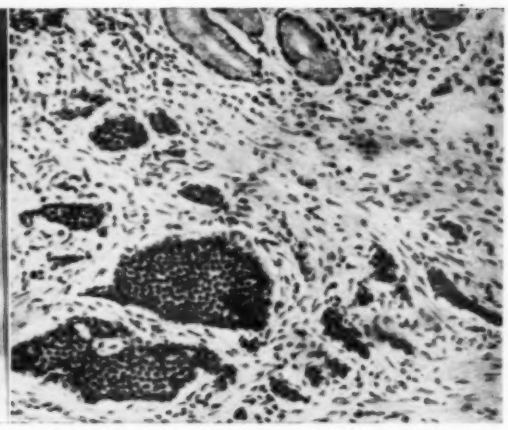
CASE REPORTS

CASE 1: A 50-year-old man was admitted to New Haven Hospital in December 1939 complaining of "grabbing pains" which began just below the umbilicus and radiated toward the epigastrium. Attacks had occurred intermittently for three weeks, were of brief duration, and came at intervals ranging from five minutes to several hours. They were followed by a residual soreness in the lower abdomen. The distress was unrelated to ingestion of food and frequently awakened the patient at night. He had some eructation and often a feeling of intestinal rumbling immediately after a spasm of pain. On two occasions he vomited normal stomach contents. During the three weeks constipation had developed, and there had been a considerable loss of weight, although the exact amount was not known.

The patient had lost 14 pounds of weight during a previous gastro-intestinal disturbance in August 1938, but the pain had then occurred more definitely after meals and not at night. An x-ray study at that time had shown an ulcer "just beyond the stomach." Some relief had been gained by strict ulcer management. The past history was otherwise of no significance.

[1] Accepted for publication in March 1942.





Figs. 1 and 2. Case 1: The x-ray film, taken five hours after the administration of barium by mouth, shows the much dilated loop of bowel, jejunum. Its distal end in the right mid-abdomen is irregular medially, due to the tumor. A few flecks of barium can be seen behind the tumor in the loop distal to the tumor. The bowel is kinked at the point of the tumor. This is characteristic of argentaffinomas. The significance of this finding was not appreciated when it was observed.

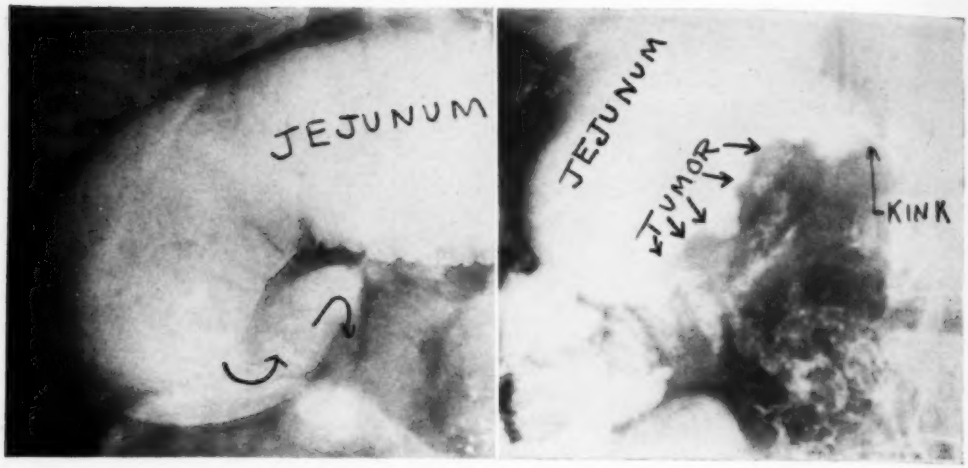
In the microscopic picture of the tumor, jejunal glands are seen at the top. The masses of dark-staining cells toward the bottom are tumor cells. They are in the submucosa and are surrounded by a great deal of fibrous tissue. This is quite characteristic of the appearance of these tumors.

On admission, the abdomen was moderately distended, with some tympanites and borborygmi. The rectus muscles gave moderate resistance but showed no spasm or tenderness. Laboratory studies, including a guaiac test on the stool, were negative. A gastro-intestinal roentgen study was made on Dec. 7, 1939. Initial fluoroscopic examination and a plain film of the abdomen showed several fluid levels in a dilated loop of the bowel high in the abdomen. The esophagus, stomach, and duodenum showed no abnormality. The proximal jejunum was not dilated. Three hours after ingestion of the barium mixture, the stomach was empty and most of the barium was in a greatly dilated loop of the jejunum (Fig. 1). On this and succeeding films a rounded shadow was seen protruding into the lumen at the distal end of the dilated loop and at this site the bowel was kinked. Beyond this point the jejunum and ileum were normal. Barium reached the cecum at the end of seven hours. At twenty-four hours some barium was still seen in the dilated jejunum but most of the meal was scattered throughout the colon. The x-ray diagnosis was partial obstruction of the small bowel presumably due to a tumor, probably benign, in the region of the distal jejunum. The preoperative impression was obstruction due to carcinoma, polyp, lipoma, or carcinoid.

On Dec. 12, a laparotomy was performed. The obstruction in the jejunum was found to be due to an annular constricting ring and a kink in the bowel at the same site. The bowel was dilated proximally and collapsed distally. The serosal surface was unbroken, smooth, glistening, and whitish gray. Numerous telangiectatic blood vessels extended in both directions from the scirrhous ring. The adjacent mesentery was indurated and several almond-sized lymph nodes could be palpated within it. Three other nodes at the root of the mesentery appeared to contain metastases. The involved segment of intestine was resected and a side-to-side anastomosis was made. The pathological diagnosis (Dr. Tenant) of the tumor in the resected bowel was carcinoid of the jejunum (Fig. 2). Convalescence was somewhat retarded by postoperative pneumonia, but the patient was discharged as improved on Dec. 31, 1939.

Case 2: A 55-year-old white housewife was seen in the University of California Outpatient Department on Jan. 13, 1941. She complained of attacks of severe cramping epigastric pain relieved by vomiting. These attacks had occurred intermittently for six months and had lasted as long as two or three weeks. For the past two months the pain had increased in severity and had been associated with a knot-like sensation in the abdomen. The attacks of pain were frequently followed by diarrhea but, while some of the stools had been dark, melena had not been noted. There was no hematemesis. The weight had decreased 50 pounds in the six months. No masses were palpable in the abdomen and the solid organs were not felt. A small ventral hernia protruded from the scar of a previous herniorrhaphy.

An x-ray study of the gastro-intestinal tract was reported by Dr. J. Irwin as follows: "There is marked dilatation of the jejunum with almost complete obstruction in the distal portion. The films



Figs. 3 and 4. Case 2: The film on the left shows the huge dilatation of the proximal jejunum. The bowel is kinked near its end and then almost completely obstructed. Fluoroscopically, it was seen to be even more kinked at the point of obstruction.

The film on the right shows the irregular tumor borders. The few tiny flecks of barium seen through the tumor are in the loop distal to it.

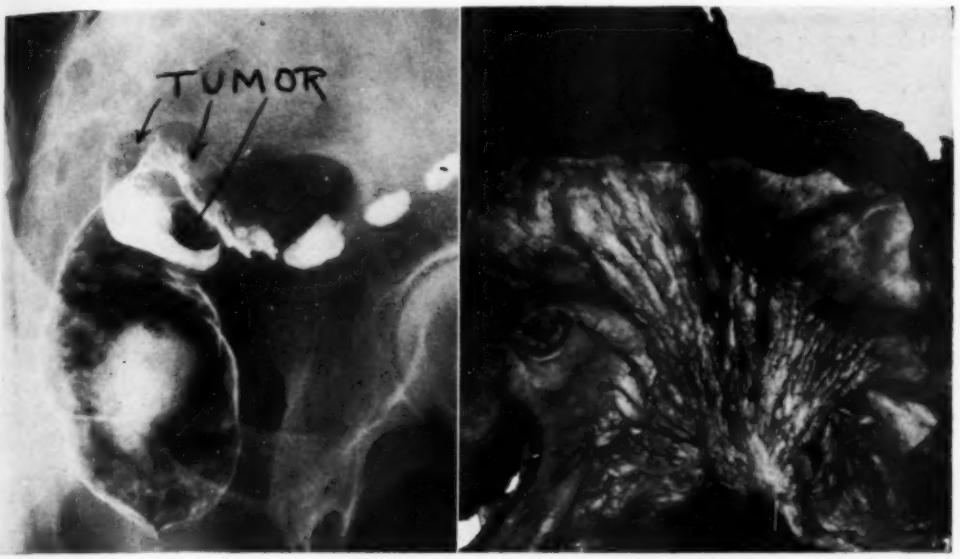
show the markedly dilated jejunum tapering down to a point beneath the liver (Figs. 3 and 4). Occasionally a defect is seen in this region, but it is not constant." The obstruction was not complete, since at twenty-four hours barium was seen in the terminal ileum and colon. Dr. Irwin stated that the changes were thought to be the result of adhesive constrictions. On re-examination of the films it was thought that a filling defect could be made out at the point of obstruction and that at this point the bowel was kinked. One of us (E. R. M.) suggested argentaffinoma as the cause of the partial obstruction because of the presence of tumor and kinking of the bowel at the same site.

A Miller-Abbott tube effectively relieved the small bowel distention but did not stop the peristaltic rushes. One stool specimen was positive for occult blood. Operation was performed on Jan. 18, 1941, by Dr. Edward Clausen, and a hard tumor, 4 cm. in diameter, was found in the mesenteric border of the upper portion of the ileum. The adjacent mesentery was studded with multiple nodules up to 3 cm. in diameter. The obstruction was caused by mesenteric retraction and resultant constriction of the lumen of the bowel. The wall of the bowel was infiltrated over an area measuring about 1.5 cm. As resection was impossible, a side-to-side anastomosis was made between the bowel just proximal to the lesion and that just distal to the lesion. A lymph node was removed for biopsy. The postoperative course was uneventful and the patient left the hospital on Feb. 1, 1941.

The pathologic report, by Dr. E. I. Bartlett, was as follows: "Grossly the specimen consists of a lymph node 0.5 × 0.5 × 3.0 cm. The cut surface is pale gray and pink and has a homogeneous cellular appearance. Microscopically the structure of the node is fairly well preserved and appears hyperplastic. In isolated areas of the margins the tissue has been replaced by small masses of compact cells arranged in circumscribed fibrous bundles. The cells are round or fusiform. The cytoplasm is eosinophilic and finely granular. The boundaries of the cells are poorly defined. *Diagnosis:* Lymph node metastasis of carcinoid tumor of small intestine (argentaffinoma)."

CASE 3.: A 67-year-old white man was first seen on the private service of Dr. Kruse at the University of California Hospital in February 1937 because of recurrent upper right abdominal pain caused by stones in the gallbladder and cystic duct. No demonstrable lesions were found in the gastrointestinal tract by the customary technic of immediate, six-, and twenty-four-hour x-ray examination. At cholecystectomy the surgeon removed the stones. No other abnormality in the digestive tract was noted at operation. The patient had had, over a period of years, "chronic indigestion" with belching, borborygmi, and abdominal pain, occurring immediately after eating and lasting several hours.

Eighteen months after cholecystectomy the patient returned, complaining of weight loss and nausea of six months' duration. The nausea seemed to be aggravated by fats in the diet. There had been some distention of the upper abdomen and belching. A routine x-ray examination of the gastro-intestinal tract showed a deformity in the duodenum suggestive of ulcer. Hypochlorhydria had been present, however, and, since the symptoms were not compatible with peptic ulcer, the patient was given



Figs. 5 and 6. Case 3: The film shows the tumor encircling the rectosigmoid. This proved to be a metastatic carcinoid, primary in the ileum. The primary lesion in the ileum had not produced enough obstruction at the time of the gastro-intestinal examination to be recognized.

The gross specimen shows the way the tumor invades the mesentery and retracts the bowel. Above is the open lumen of the ileum. Below is the fan-shaped mesentery filled with tumor nodules. At the junction of the mesentery and the serosa one sees the effect of the contraction of the fibrous tissue of the tumor. The bowel can be seen to be crinkled and folded upon itself. In the fresh specimen this portion of the bowel appears sharply bent upon itself. The primary tumor is hidden within the lumen of the bowel opposite the center of the mesenteric fan.

dilute hydrochloric acid, bile salts, and a bland diet. As the general condition improved and the weight increased, the red blood count and hemoglobin rose.

In July 1939 a transurethral resection of an obstructing prostatic bar was performed. Postoperative pneumonia followed, for which sulphanilamide was given in customary doses. A vicious diarrhea and symptoms of myocardial insufficiency developed. Subsequently the major symptom was frequent and loose stools. These could be partially controlled by tincture of opium. There was much abdominal gas but no pain. No abdominal or rectal masses could be felt and the rectal mucosa was normal in appearance.

In January 1940 the patient began to have loose stools at night as well as during the day. X-ray studies revealed a deforming and obstructing lesion at the rectosigmoid junction (Fig. 5). A small sigmoidoscope was passed to its full length (10 inches) on several occasions, but no lesion could be seen within the lumen nor could the constriction demonstrated by x-ray be identified. In February 1940 a laparotomy was done. The peritoneal surface was studded with nodules and a mass was seen lying posteriorly and laterally in the left side of the pelvis. The tissues were matted so that the "large bowel tumor" could not be seen clearly. The tumor was deemed too extensive for removal. Biopsy of a mesenteric node was reported as metastatic carcinoma in the mesentery with "atypical neoplastic epithelial cells." The immediate postoperative course was uneventful.

The patient returned in October 1940 with general abdominal pains, nausea, persistent vomiting, obstipation, and weight loss. The abdomen was hard and moderately distended. Plain films showed no evidence of bowel obstruction. The clinical diagnosis was complete low obstruction of the small bowel. The patient gradually became dehydrated, emaciated, and irrational, and died on Oct. 22, 1940.

Postmortem examination failed to disclose any primary lesion at the rectosigmoid junction, but there was a circumferential infiltration of the serosa at that point with hard gray tumor tissue. The omentum and mesentery were devoid of fat and matted together by firm white nodules (Fig. 6), which also spread over the visceral and parietal peritoneum. About 60 cm. from the ileocecal valve was a nodule, 3 cm. in diameter, which protruded into the lumen of the ileum. The lumen at this point was partially obstructed due to the presence of the intraluminal mass and the knuckling of the bowel as a result of the infiltration of the deeper intestinal coats and the mesentery. No metastases were seen in the liver except such as had infiltrated from the serosal surface. A small lymph node along

the inferior mammary vessels under the sternum contained tumor cells. Otherwise, no extension into the thorax was found. The microscopic study proved the neoplasm to be an argentaffinoma.

DISCUSSION

Carcinoids have been the subject of extensive discussion by pathologists. Forbus (6) gave an excellent review of the literature up to 1925. Ariel (1) presented five theories as to the origin and nature of carcinoids of the intestinal tract: (1) that they are true carcinomas; (2) that they are neoplasms related to basal-cell carcinoma of the skin; (3) that they are embryonal remnants of malformations developed from pancreatic rests; (4) that they are neoplasms of the sympathetic nervous system; (5) that they are of argentaffin cell origin, their progenitors being the cells which lie in the bases of the crypts of Lieberkühn. The majority of writers agree that carcinoids originate in the argentaffin cells, as first suggested by Masson (9). Collins (4), in a review of the literature, reported sixteen theories concerning the origin of carcinoids.

The pathological picture of argentaffin tumors is characteristic. Grossly the benign lesions consist of pale yellow submucosal nodules which on section show white interlacing bands. The cells are small and polyhedral, with indistinct borders. The nuclei are vesicular with prominent nucleoli. The cytoplasm is finely vacuolated and contains cholesterol, lipids, and silver-staining granules. On the basis of their affinity for silver, the tumors have been designated argentaffinomas. The primary lesions do not enlarge greatly toward the lumen but remain chiefly in the submucosa. When malignancy supervenes, the tumor invades the wall of the bowel and extends into the mesentery. It may spread over the peritoneum. Kinking or knuckling of the bowel occurs at the site of the lesion. This seems to be due to the contraction and growth of the fibrous stroma of that portion of the tumor that has invaded the mesentery. This specific characteristic of argentaffin tumors facilitates radiological diagnosis.

In 7,733 necropsies reported from several clinics the incidence of carcinoids was 0.6 per cent. The commonest of all sites as indicated by surgically removed specimens is the appendix, with an incidence of 0.4 per cent. The next most common site is the ileum. Since 1930, about 250 carcinoids of the small bowel have been reported. Busser (2) and Warren (13) have noted concomitant tuberculosis. Argentaffinomas occur equally often in males and females and have been reported at all ages above ten days. Most of the appendiceal tumors are found between the ages of twenty and thirty, whereas those in the small bowel usually occur during the fourth and fifth decades.

Carcinoids were originally separated from carcinomas by Oberndorfer (10) on the basis that they are usually multiple and benign; that the cells occur in large undifferentiated masses, although occasionally acinus formation is present; that they show no tendency to infiltrate or metastasize; that they are of slow growth and harmless; that they lie in the submucosa; that the muscularis mucosae is always present; finally, that the stroma is smooth muscle having its derivation from the muscularis mucosae.

Porter and Whelan (11) and Wyatt (14), on the other hand, have collected 68 cases of carcinoids of the gastro-intestinal tract with metastases. The distribution of the primary tumors was as follows: stomach 1, jejunum 2, ileum 39, small bowel (unspecified) 9, appendix 14, colon 3. Twenty-five per cent of the carcinoids in the small bowel reported by Kross (8) and 24.4 per cent of those reported by Humphreys (7) were malignant. The metastases have almost invariably been found in the regional lymph nodes; in a few cases they have also spread to the liver. Carr (3) reported a case in which metastases occurred in the vaginal vault, the primary lesion being in the ileum. Collins *et al.* (4) recorded a case in which the lesion originated in Meckel's diverticulum. In one instance the tumor arose in the sigmoid and metastasized to the lung and in another

a carcinoid of the small bowel showed a secondary nodule in the testicle (5). The highest percentage of metastases is found in primary carcinoids of the stomach and colon (Raiford, 12). The greatest incidence of malignant carcinoids is in the sixth and seventh decades, although cases have occurred as early as the third and as late as the ninth decade. The average age of patients with malignant carcinoids of the small bowel is 57.2 years. Because of their slow growth these tumors carry a fair prognosis even though invasion may have occurred.

Small bowel carcinoids produce no symptoms as long as they remain localized in the submucosa and they are usually incidental findings at necropsy. When they do invade the serosa, they cause symptoms of chronic intestinal obstruction of varying degrees. When patients complain of chronic peri-umbilical pain or of frequent loose bowel movements over a long period of time, not adequately explained by the usual studies and resistant to therapy, a special x-ray study of the small bowel should be made, with hourly observation of the passage of barium through the intestine. The presence of tumor of the small intestine, with shortening of the mesenteric attachments and kinking of the subtended loops, should arouse the suspicion that this slowly spreading, infiltrating lesion may be present. The mechanism of obstruction depends upon the ability of the tumors to invade the mesentery and to produce adhesions and kinking of the bowel, rather than upon the size of the tumor itself.

SUMMARY

Three cases of malignant argentaffinoma of the small bowel are reported.

The origin, clinical features, pathology, and incidence are discussed. The roentgen finding of tumor at a point of kinking and partial obstruction of the small bowel is believed to be a highly suggestive sign of these tumors.

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Perforation of Peptic Ulcer[1]

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PERFORATION is the most serious complication of peptic ulcer and may also be the first definite evidence of ulceration. Portis and Jaffe, reviewing 9,171 consecutive autopsies, found 457 peptic ulcers, of which 120 had perforated. In an extensive review of the literature Speck (quoted by Feldman) estimated that 10 per cent of all peptic ulcers perforate. Feldman collected 3,897 examples of perforation, of which 3,656 were in males. Uncommonly, perforation may result from an ulcerating cancer of the stomach.

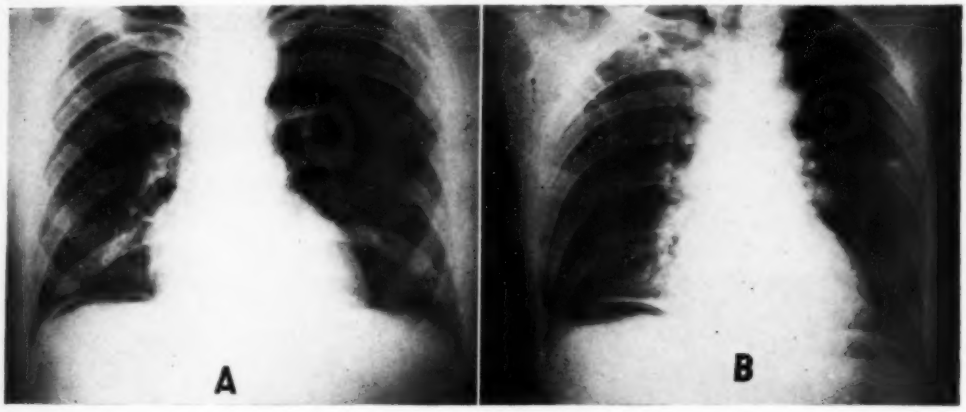

Fig. 1. Films made with the patient upright, showing free air under both halves of the diaphragm, resulting from (A) acute perforation of a duodenal ulcer; (B) acute perforation of a gastric ulcer.

The majority of ulcerative lesions are on the anterosuperior wall of the duodenum and stomach near the pylorus. Anatomically the anterior wall is more exposed to the general peritoneal cavity than is the posterior wall. Lesions on the posterior wall and those along the curvatures are well or partially protected.

Perforation is more frequently seen in younger than in older patients. Generally speaking, it is more common in duodenal than in gastric ulcers, although statistical studies are not entirely in accord on this point. According to Dillon (quoted by Cecil), perforation occurs in about 5 per cent of duodenal ulcers and in less than 2 per cent of gastric ulcers. Shawan collected 277 examples of perforation, of which 39 were in the pylorus, 55 in other parts of the stomach—mostly the pars media, along the lesser curvature—and 132 in the duodenum. Of this series 87 per cent occurred between the ages of twenty and fifty. Of Johnson's series of 1,149 perforations, 56 per cent were in the stomach and the remainder in the duodenal bulb.

Of 211 cases of gastroduodenal perforation in the Charity Hospital series, De Bakey found 44 per cent near the lesser curvature, in the region of the junction of the pars media and pylorica, and 40 per cent in the bulb. Ninety-five per cent of all the cases were on the anterior wall.

At operation it may be difficult to distinguish between duodenal and prepyloric

[1] From the Welfare Island Dispensary of the Department of Hospitals of the City of New York (Richard A. Rendich, M.D., Citywide Director of Radiology). Thanks are due Doctor Rendich for some of the material. Accepted for publication in December 1940.

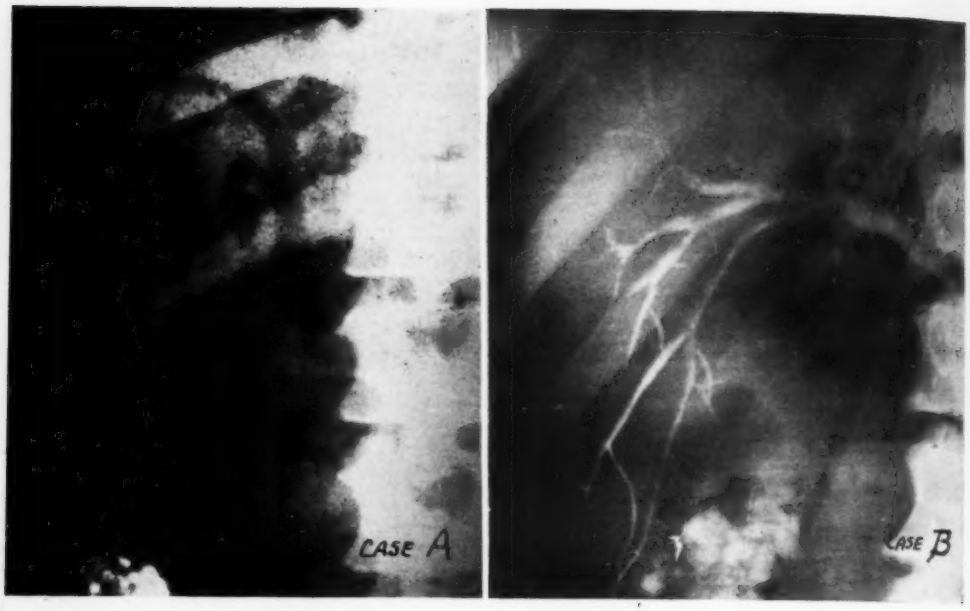

Fig. 2. Spontaneous internal biliary fistulae. A. Simple abdominal film showing air in the bile ducts due to chronic perforation of a duodenal ulcer (courtesy of Dr. Charles Gottlieb). B. Barium in the bile ducts due to chronic perforation of a duodenal ulcer.

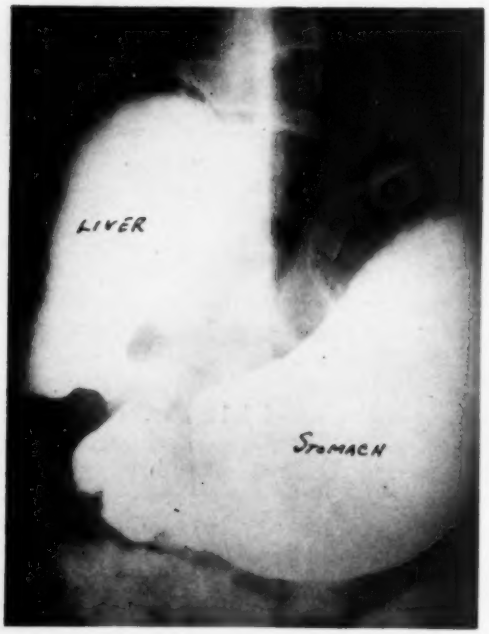

Fig. 3. Spontaneous internal fistula due to a very chronic perforation of a duodenal ulcer into the liver, with destruction of the liver substance and the formation of a large pocket bounded by the liver capsule.

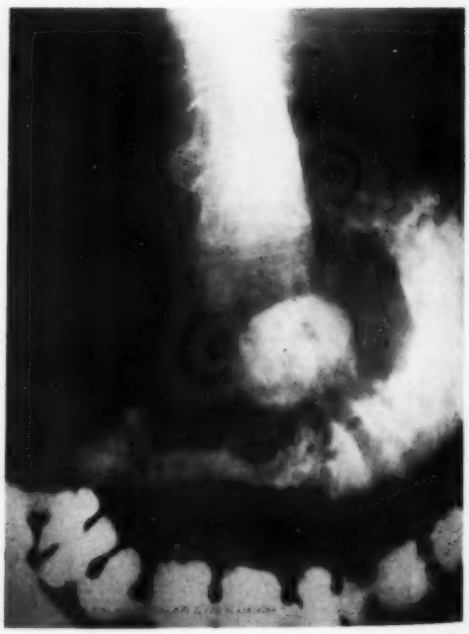

Fig. 4. Benign ulcer of the lesser curvature of the pars media with perforation into the lesser peritoneal sac and the formation of a pocket connecting with the lesser curvature.

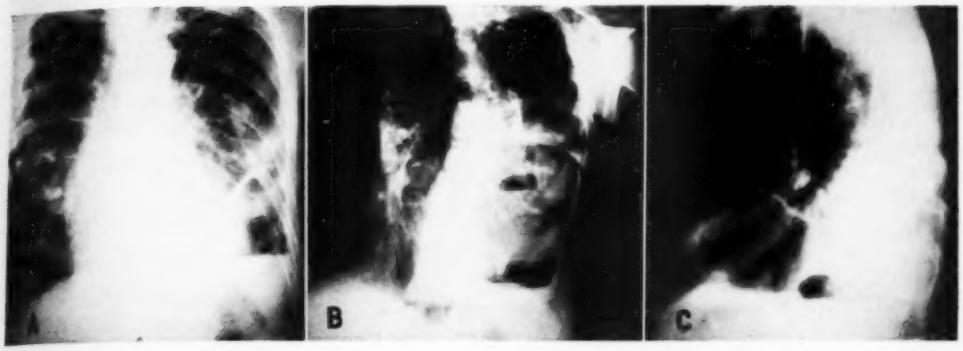

Fig. 5. Chest roentgenograms in the (A) anterior posterior, (B) left oblique, and (C) left lateral projections, demonstrating several loculated hydropneumothoraces with partial erosion of the 8th and 9th ribs. The presence of air in the pleural cavity and profuse expectoration led to a diagnosis of a malignant growth of the pleura with a bronchopleural fistula. At autopsy a gastropleural-bronchial fistula was found. A cancer of the cardiac end of the stomach had perforated through the left half of the diaphragm into the left pleural cavity and subsequently into the lower left portion of the bronchial tree.

ulcers; in such cases Mayo used the pyloric vein as a demarcation point.

CLASSIFICATION

There are three types of perforation: acute, subacute, and chronic.

Acute perforation produces a severe prostration. Of all the sudden catastrophes to which an ulcer-bearing patient is liable, it is the most ominous. Moynihan, Sherren, and Walton have observed that an ulcerating lesion which undergoes acute perforation is usually chronic, and that it is the perforation that constitutes the acute process. The perforation is usually, though not always, small, often only the size of a pinpoint. Acute perforation occurs most frequently from ulcers on the anterior wall.

Subacute perforation is characterized by an attack of sudden epigastric pain, which is severe, but less so than in acute perforation, and from which recovery occurs. Most often there is a slight leakage of contents with a spontaneous sealing or plugging of the perforation, and subsequent recovery under non-operative treatment.

Chronic perforation is a common complication and, according to Eusterman and Balfour, is noted in one of every four cases verified surgically. As the ulcerative process reaches the serosa, an inflammatory reaction occurs, as a result of which the base of the ulcer becomes adherent to a neighboring organ, as the pancreas or liver or less frequently the gallbladder or colon. Once a firm attachment is established, penetration and ulceration may continue into the substance of the involved organ. Rarely, a fistulous connection is established between the stomach or duodenum and a neighboring hollow viscus, as the gallbladder or the colon, or to the skin. Under certain conditions, perforation may take place into the lesser sac with the formation of a localized abscess. McCrae states that liver penetration is exceptional. Chronic perforation occurs frequently from ulcers on the posterior wall. Eusterman and Balfour state that chronic perforation may occur without any symptoms, a phenomenon attributed to the slowness of the perforation.

ROENTGEN DIAGNOSIS OF PERFORATED PEPTIC ULCER

Acute perforation may be manifested on a simple abdominal film, made in the upright or semi-upright position, by the presence of free air under one or both halves of the diaphragm, or it may be indicated by the occurrence of free air between the right lateral abdominal wall and the liver in anterior-posterior films made with the patient in the left lateral recumbent position. In the presence of general

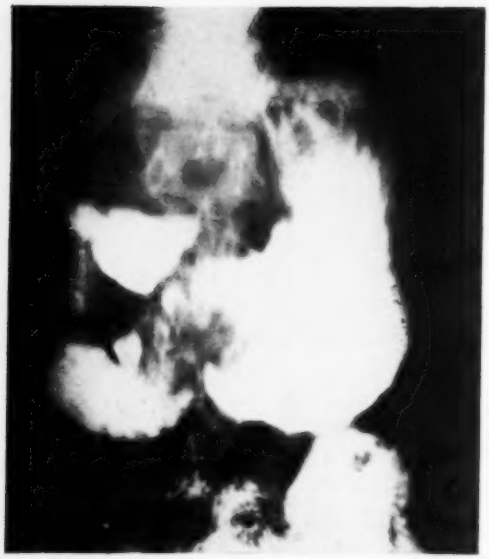

Fig. 6. Cancer of the pylorus with extraluminal barium in the region of the pancreas. Autopsy revealed perforation into the pancreas.

peritonitis the bowels may be in a state of paralytic ileus.

The subacute or chronic forms are not usually demonstrable on a simple abdominal film, though exceptionally, as shown in Fig. 2-A, this is possible. Usually, study after the administration of barium sulphate is necessary. Even then a perforation may not be demonstrated if it is sealed off or plugged by food, mucus, or a blood clot. When it is visualized, it may be manifested (1) by a barium-containing pocket in the region of the lesser peritoneal sac connecting with the lesser curvature of the stomach, (2) by an extraluminal collection of barium in the pancreatic region or in one of the subphrenic areas connecting the stomach or duodenum, or (3) by intestinal fistulae connecting with the liver, bile ducts, pancreas, or transverse colon, or, very rarely, by an external fistula to the skin. The internal fistulae form more or less gradually; many are asymptomatic and they are sometimes discovered incidentally during examination of elderly people.

We have had two ulcerating cancers of the stomach go on to chronic perforation: one in the pyloric portion, perforating posteriorly into the pancreas, and one in the cardiac end, perforating through the left half of the diaphragm into the left pleural cavity and subsequently into the lower left portion of the bronchial tree, forming a gastro-pleural-bronchial fistula.

DIFFERENTIAL DIAGNOSIS

Free air under one or both halves of the diaphragm is not necessarily indicative of a perforated ulcer. It may be due to a recent laparotomy, a peritoneoscopy, a pneumoperitoneum, or a Rubin test. Free air may also be present following an ordinary paracentesis of the peritoneal cavity or after withdrawal of fluid from the chest if the needle has penetrated the diaphragm. Cases have been recorded in which pneumoperitoneum was found without known cause. In such instances, in female patients, speculation has favored air intake through the generative tract, possibly facilitated by knee-chest exercises.

Liver abscess with gas-forming bacilli, involving the uppermost portion of the liver, in which a gas bubble is demonstrable capping a fluid level, in the upright posture on the right side alone, is also to be differentiated. In these cases the gas bubble is not likely to appear just below the right diaphragmatic leaf centrally placed; nor is it likely to assume the same shape as the undersurface of the diaphragm. The gas will probably be localized in an eccentric position, and its movement on change of posture will be limited to within the radius of the abscess, while free air under the diaphragm can usually be readily shifted by change of position.

The accompanying illustrations demonstrate the types of perforation we have encountered and serve to illustrate the diagnostic roentgen features.

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CASE REPORTS

Osteoid-Osteoma of the Astragalus[1]

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The so-called osteoid-osteoma, described by Jaffe (1) in 1935 and, more extensively, by Jaffe and Lichtenstein (2) in 1940, is a solitary, benign neoplasm involving spongy or cortical bone. It has been recognized in the extremities, more often the lower, and

Fig. 1. The lateral roentgenogram of the right foot reveals a sharply defined radiolucent area, oval in shape, near the upper surface of the neck of the astragalus, its superior portion elevating the overlying intact cortical bone like a blister. The surrounding cancellous bone shows increased density, but there is no periosteal or adjacent soft-tissue reaction.

in the vertebral column, but not yet in the ribs, sacrum, innominate bones, and skull bones. This lesion may be misinterpreted, clinically and roentgenographically, as chronic osteomyelitis or bone abscess. The diagnosis should be considered in an adolescent or young adult with localized pain, with or without localized swelling, of at least several months' duration, unassociated with local heat or bouts of fever, and with normal clinical laboratory findings. The histologic features of osteoid-osteoma are distinctive and unlike those of any other classified lesion of bone. Local excision of the tumor results in immediate and complete recovery.

CASE REPORT

A 16-year-old colored male complained of increasing pain and swelling of the right ankle of four months' duration. There was no definite history of trauma. Examination of the right foot revealed slight swelling and tenderness on the anterior surface in the ankle region. The temperature, pulse, and respiratory rate were normal, as were repeated blood counts and urinalyses. The blood Wassermann and Kahn tests and an intradermal tuberculin test were also negative.

A lateral roentgenogram of the right foot was reported by the radiologist as "negative." It revealed an oval, sharply defined, radiolucent area near the upper surface of the neck of the astragalus, its superior portion elevating the overlying intact cortical bone like a blister. There was some increase in density of the surrounding cancellous bone, but no periosteal or adjacent soft-tissue reaction (Fig. 1).

The lesion was exposed through an anterolateral incision and was excised, together with the overlying cortex and adjacent sclerotic cancellous bone. The wound was closed without drainage and healed *per primam*. Smears, culture, and guinea-pig inoculation of material taken from the lesion were negative. The patient experienced immediate relief of pain, although some swelling of the right ankle region has persisted.

Histopathologic Features: Grossly, the tumor was soft and reddish brown in color. Microscopically, it was composed predominantly of trabeculae and patches of osteoid tissue, lined by osteoblasts and set in a substratum of highly vascular osteogenic connective tissue that was sprinkled with numerous osteoclasts. A few of the osteoid trabeculae were undergoing early calcification and transformation into atypical bone (Figs. 2 and 3). The tumor tissue was sharply delimited from the compact trabeculae of the adjacent bone.

DISCUSSION

The roentgenographic picture in osteoid-osteoma demonstrates two features—the neoplasm proper and the reaction of the surrounding bone. Early in its development, the tumor is indicated by a circular or oval radiolucent or rarefied area of bone. Later this nidus becomes opaque as calcification and ossification

[1] Accepted for publication in February 1942.

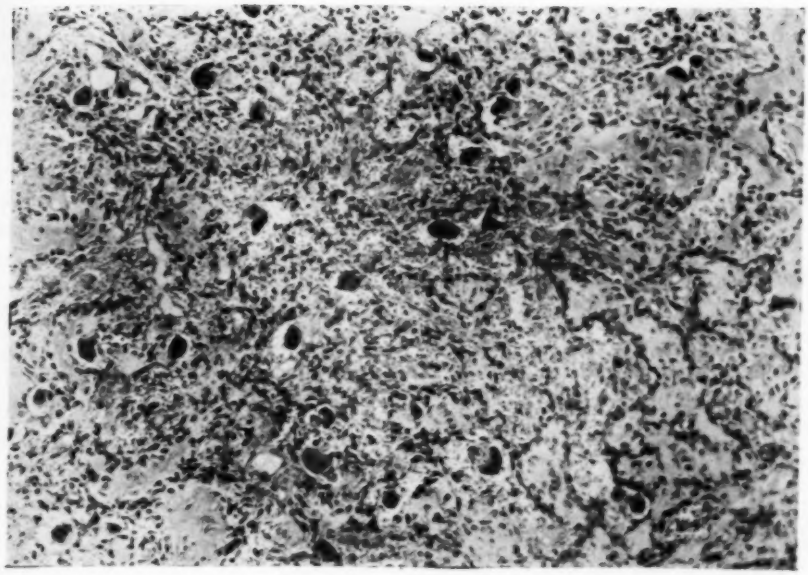

Fig. 2. Section of the osteoid-osteoma, showing numerous osteoid patches in a substratum of highly vascular, proliferating, osteoblastic connective tissue containing numerous osteoclasts. ×125.

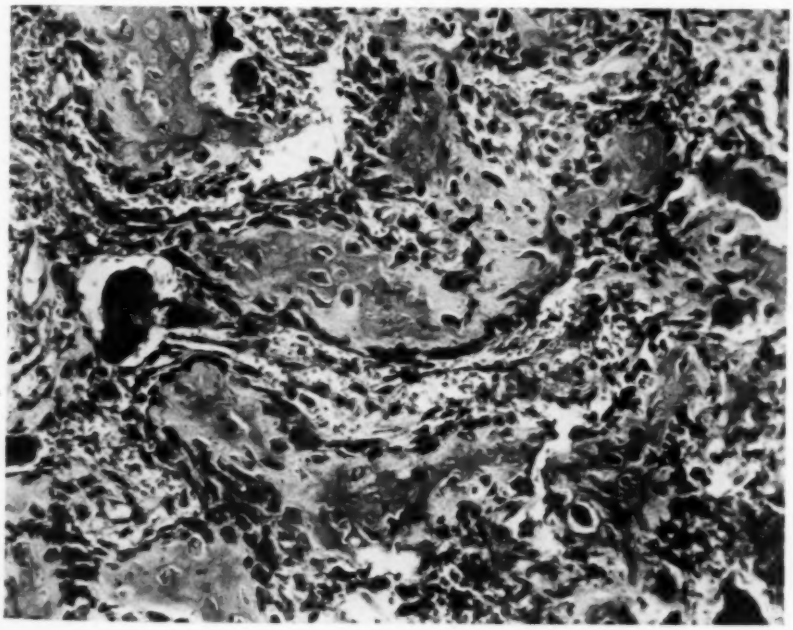

Fig. 3. Another area in the section from which Fig. 2 is taken, showing osteoid trabeculae lined by osteoblasts, undergoing early calcification and transformation into atypical bone. The substratum of highly vascular, osteogenic connective tissue contains several osteoclasts.

progress, but it may still remain distinct from the surrounding dense bone, from which it is demarcated by a zone of relative radiolucency. In the small bones, as in the case here reported, the position of the lesion may be superficial and it may even erode the overlying cortical bone and elevate (but not penetrate) the periosteum without necessarily inciting it to excessive proliferation of new bone. In the cortex of a long bone shaft, an extensive osteosclerosis is stimulated, and there may be considerable bony proliferation on the periosteal or medullary surfaces, depending on the location of the lesion. The osteosclerosis in these cases may dominate the picture and overshadow the primary lesion, leading to a mistaken diagnosis of so-called "sclerosing non-suppurative osteomyelitis of Garré" or "intracortical-bone abscess" (2, 3).

The pathologic features of osteoid-osteoma are distinctive and have been interpreted by Jaffe as those of a benign osteogenic tumor of bone. Early, the tumor consists of proliferating, vascular osteoblastic tissue, with a scattering of osteoclasts. (The relatively large number of osteoclasts throughout the lesion in the writer's case led to its misinterpretation as a giant-cell tumor of bone.) In the more mature form, there appear areas of osteoid tissue in various stages of calcification. When fully developed, the lesion is composed of compact trabeculae of highly calcified atypical bone with rather vascular and cellular intertrabecular tissue. There is increased density of the trabeculae of the surrounding spongy or cortical bone.

SUMMARY

An instance of osteoid-osteoma, a benign osseous neoplasm, that involved the astragalus is reported, with the main purpose of directing further attention to the original communications on this specific lesion of bone.

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EDITORIAL

Howard P. Doub, M.D., Editor

John D. Camp, M.D., Associate Editor

The Linear Thoracic Paraspinal Shadow

A slender vertical line of demarcation is often seen in anteroposterior or sagittal roentgenograms of the bony thorax and upper abdomen. This line lies on the *left* side of the lower two-thirds of the thoracic spine and sometimes continues as far down as the plane of the first two lumbar segments. The shadow is frequently an enigma to radiologists and other clinicians viewing such roentgenograms. It is not visible on all films or projections of this portion of the body but is observed with such frequency that it must be the result of variation in the course or position of a normal structure situated therein.

The density of the shadow is not bony. It is too incomplete to be caused by a unilateral spinal ligament, even if such a structure were anatomically possible. The linear objects that commonly occupy both the thoracic and abdominal regions and run continuously between these areas are the large vessels. These structures contain blood, and are sufficiently thick to cast a shadow on a roentgenogram provided they are adjoined or surrounded by material of different density.

The descending aorta is not the source of this shadow, since its location is not exclusively vertical and paraspinal, and indeed its left lateral margin can often be seen lateral to this paravertebral shadow. The inferior vena cava likewise is not to be considered, owing to its dextral location and shorter course.

A vascular structure, inconstant in location and development, which not uncommonly lies in this region of the body is the hemiazygos vein. This vein arises in the left ascending lumbar vein or in the left renal vein and enters the thorax through an aperture in the left crus of the diaphragm. It ascends on the left side of the vertebral column to the level of the eighth thoracic vertebra, passes across the column behind the aorta, esophagus, and thoracic duct to end in the azygos vein.

Deviation from standard venous patterns or distributions is one of the commonest developmental anomalies. It is quite possible that in a significant number of persons the azygos vein is small and the hemiazygos assumes a portion of its function in venous drainage. In this group the enlarged and elongated *hemiazygos vein* may cast its shadow to the left of the spine to produce the vertical linear shadow referred to in our opening paragraph. This editorial is written with the suggestion that this finding be referred to as the "left thoracic paraspinal shadow," and that its frequency be noted by various radiological observers. In this manner its true incidence may be ascertained, and its apparent nature confirmed.

L. H. G. AND I. J. M.

Radiologists and Fractures

One of the primary uses of x-rays in diagnostic procedures is the examination of bones for the detection of fracture. The constant, daily use of this form of examination tends to produce a certain casualness or over-confidence on the part of those making the films and particularly of those responsible for their interpretation.

There are two general types of opinion about the roentgen diagnosis of fracture,

particularly in the smaller bones of the extremities: first, that "anyone" can "read" a fracture; second, that the specialist (radiologist) is uniquely expert and cannot overlook or misdiagnose so simple a thing.

It can readily be shown that the first opinion is not correct. Instances are legion in which a referring physician has interpreted his patient's films (in the darkroom, partially processed!), reassured the patient, and sent him on his way—but has later been chagrined to find mature interpretation resulting in a diagnosis of fracture. Obviously, this is not the fault of the radiologist but the "x-ray" tends to be blamed and the method to become falsely discredited.

The second opinion, that an x-ray specialist cannot overlook a fracture, would come closer to being correct if radiologists would pay closer attention to the positioning of patients and the exact technic used in the examination of a suspected fracture case. Short cuts to reduce expense are false economy. Single views (even when requested by the referring physician) without studies in the opposite plane lead eventually and inevitably to the overlooking of lesions. An anteroposterior and a lateral view often constitute adequate study of a part, but oblique projections are frequently needed as well, especially in "simple" areas like the metacarpal and metatarsal regions. Stereoscopic films, especially when viewed with the magnifying hand stereoscope, may be invaluable.

One must insist on the best possible quality of roentgenograms in all bone work. Detail in the films is more important than contrast. Motion of the part during an exposure requires that it be repeated. To maintain his reputation the radiologist cannot do without the advantages of superlative technic.

Another road to pitfalls in fracture diagnosis, often traversed by young radiologists, is failure during their period of training to put a proper amount of time and effort into the study of fracture cases. House officers in radiology become engrossed in finding small gastric carcinomas, and in differentiating between Boeck's sarcoid and coccidioidomycosis, while they spend little time in the refinement of osteologic examination and interpretation. All too often their first diagnostic blunder in private practice turns out to be the missing of a small fracture in a carpal navicular bone. And while the specialist may be forgiven for overlooking a small gastric carcinoma, he is *never* excused for missing a fracture.

The late distinguished Dr. E. A. Merritt pointed out that osteologic examinations still constitute the major portion of the clinical practice of radiology. It therefore behooves us to be as competent as possible in this, our major field!

L. H. G.

Radium Protection During Air Raids

Attention is called to the Handbook issued in May by the National Bureau of Standards (Handbook H38) on Protection of Radium during Air Raids. This was prepared by a Committee headed by Dr. L. F. Curtiss of the Bureau of Standards and including Dr. G. Failla, Dr. John E. Rose, Dr. Curtis F. Burnam, Dr. Harrison S. Martland, Dean George B. Pegram, and Lt. Col. Sherwood Smith.

The intent of the Committee's recommendations is not so much to minimize the loss of radium but rather to prevent, so far as can be foreseen, danger to human life inherent in the peculiar properties of that element. A certain hazard exists in the handling of radium under normal conditions. Its dispersal as a result of a possible explosion involves a considerable increase of this hazard.

In discussing the protection of radium from dispersal as the result of the impact

of explosive bombs, the Committee has considered separately the three usual types of container.

(1) Sealed metal tubes and needles housed in modern steel and concrete structures and stored with the precautions customary under peace-time conditions may require no further protection. It is important, however, that they be kept at least four stories below the roof in tall buildings. Where structural protection is slight, the radium may be kept in a steel safe with walls $1^1/_2$ inches in thickness (equivalent to $^3/_4$ inch of lead), or in steel cylinders with walls of the same thickness and closed with a screw plug, or it may be stored in a block of reinforced concrete, 5 to 7 feet on each edge, with a steel pipe of suitable diameter mounted centrally and extending to the center of the block.

(2) Since the radium in radium bombs is already surrounded by sufficient dense material to prevent disruption of the tubes and dispersal of the radium under the severe impact of an explosion, no measures are suggested for its protection beyond those for radium tubes in general.

(3) Radon plants offer a special problem. It is especially important that the lead-lined metal cup surrounding the glass radium flask be protected against jarring and consequent displacement. For this purpose the application of a plaster-of-paris cast filling the radon safe to about the height of the metal cup is suggested. The safe itself should be so anchored as to prevent motion in any direction. The glass tubing which comes through the top of the safe should be reinforced by steel straps.

It is conceivable that under certain conditions the safe may overturn, and yet the radium flask and even the connecting tubing inside the safe remain intact. Under these conditions it is highly desirable to prevent radium solution from leaking out of the safe, and to this end means should be provided to insure breakage of the glass tubing near the center of the safe in case it should overturn suddenly. A special arrangement to insure this result is illustrated. Packing with absorbent cotton or similar material to hold the spilled solution within the safe is another precaution. Provisions are also outlined for the protection of the radon apparatus room and the installation itself against flying missiles.

To insure protection of patients undergoing radium treatment at the time of a raid, four suggestions are made:

1. A large tag of distinctive color (red) with the word "Radium" on it should be attached to the bed or to the patient himself at the time radium is applied.

2. In case of an air-raid alarm, bed patients with radium should be moved to the safest part of the building, without removing the radium.

3. In the case of ambulatory patients, radium should be removed before they are taken to the part of the building assigned to them. The radium should be put immediately in a protective container and taken care of in accordance with the general provisions outlined in the report.

4. Patients undergoing radium "bomb" treatment should be evacuated to the assigned place. If the apparatus is provided with a device which shuts off the radiation beam, the nurse or technician administering the treatment must set the radium bomb in the closed position as soon as the air-raid alarm is received.

It is recommended that rooms in which large quantities of radium are kept be evacuated by all personnel during an air raid. This is especially important in the case of radon plants; since the radium, under these conditions, is in solution and the safe is of light construction, it is suggested that adjacent rooms also be evacuated.

A special section is devoted to salvage of dispersed radium, which should be done under the direction of a competent physicist.

It is impossible to present here all the details covered in the Handbook, which should be in the possession of everyone concerned with the care of radium. Copies are available from the Superintendent of Documents, Washington, D. C. Price 10 cents.

A.M.A. Clarifies Medical Practice in Hospitals

Patients receiving the services of a radiologist during hospitalization should receive a bill for professional services rendered in the name of the radiologist. This is the purport of a resolution introduced by Dr. E. H. Skinner for the Section on Radiology, and unqualifiedly endorsed by the House of Delegates of the American Medical Association at its June meeting in Atlantic City. While the resolution pertains to all types of medical services and the general problem of practice in the hospital, its provisions will be of special interest to radiologists.

Referring to the continued encroachment of hospitals upon the practice of medicine, the resolution called upon the House of Delegates to reaffirm previously enunciated principles opposing the practice of medicine by hospital corporations through the medium of employed physicians, and provided that "all fees for medical services rendered in hospitals should be collected by or on the account of the physician rendering such service." The complete text of the resolution follows:

Whereas, the House of Delegates approved a resolution, introduced by Dr. Harry H. Wilson, at the 1941 session, instructing "the Board of Trustees of the American Medical Association to confer with similar committees representing the American Hospital Association and the Protestant and Catholic hospital associations of the United States, the conjoint committees to study and submit reports to their respective national bodies, in which would be outlined platforms or principles designed to clarify the relation of medical services that may be offered in prepayment hospitalization and similar plans, the same to be in line with the basic principles laid down in the past by the House of Delegates and other authorities of the American Medical Association. . . ."; and

Whereas, the Board of Trustees was requested in the same resolution to "proceed to these matters as expeditiously as may be possible"; and

Whereas, evidence of continued encroachment of hospitals into the practice of medicine are manifest in numerous group hospitalization plans which offer certain medical services on a service basis as a part of hospital care, and in plans adopted by numerous hospitals which include certain medical services in an "all-inclusive" per diem rate for hospital care; now therefore be it

Resolved, that the House of Delegates reaffirms the principles enunciated in official resolutions over a period of many years opposing the practice of medicine by corporations or the interjection of a third party into the personal relationship and financial transaction between doctors and patients; and be it further

Resolved, that hospital corporations should not be permitted to engage in the practice of medicine through the medium of employed physicians or to enter into contracts with any individual, group, or agency, whereby the hospital agrees to furnish any medical services; and be it further

Resolved, that, to the end that hospitals be discouraged from offering the services of licensed physicians to patients on a contract or service basis, all fees for medical services rendered in hospitals should be collected by or on the account of the physician rendering such service, and all physicians concerned in the care of a patient should give or send directly to the patient or other responsible party a statement showing charges for professional services rendered; provided, however, that an exception to the foregoing principle may be made in the case of a formally organized partnership of physicians which acts in the capacity of an individual; and be it further

Resolved, that the definitions of medical service and hospital service as applied to the principles stated herein shall be consistent with those applied in previous declarations of the House of Delegates in which medical services are construed as the services rendered by licensed practitioners of medicine, and hospital service as limited to hospital accommodations such as bed, operation room, medicines, surgical dressings, and general nursing care; and be it further

Resolved, that the Board of Trustees be urged to proceed to the clarification of these problems as requested by the House of Delegates at its last annual session.

The Reference Committee on Legislation and Public Relations, to which it was referred, reported to the House of Delegates that the resolution was consistent with principles previously stated by the House and recommended its adoption. The House adopted the report without dissent or debate.

Numerous physicians, including several

delegates, appeared before the reference committee in behalf of the resolution. During the hearing it was pointed out that the recommendations contained in the resolution would not prohibit hospitals from collecting for radiological charges at the cashier's office, but would require that such charges be rendered on the bill-head and in the name of the physician-radiologist. By separating the identity of the physician from the hospital, the reference committee was told, there would be less tendency for hospitals to attempt to include radiological services as a part of hospital care in group hospitalization or inclusive-rate plans.

Also considered by this committee was a resolution introduced by Dr. Lyell C. Kinney, delegate from California, pertaining to payments by insurance companies for medical services rendered in the hospital. The text of the resolution as introduced, follows:

Whereas, it is desirable that physicians and insurance companies cooperate to the fullest extent, especially in the interest of persons covered by health and accident insurance; and

Whereas, a serious situation has arisen in the administration of certain health and hospitalization schemes whereby medical services are being billed under the term "hospital services" and are being paid for by insurance companies as they are labeled hospital services; and

Whereas, the continuation or extension of such practices will inevitably lead to the inclusion of any type of medical service under the label "hospital service," at the convenience of the corporations involved and to the detriment of medical care; now therefore be it

Resolved, that the House of Delegates of the American Medical Association hereby requests insurance companies to cooperate with the organized medical profession to the end that hospitalization policies shall include only hospital benefits. If the inclusion of indemnification for medical services, such as surgery or radiology, is desired, then payment of such shall be made only on receipt of certified statement from a physician that he has rendered such. Fees for medical services should be paid to physicians *via* indemnity to the assured, or by check payable jointly to assured and physician. This practice should be maintained irrespective of whether a hospital chooses to bill for medical services as a part of its hospital bill; and be it further

Resolved, that the House of Delegates of the American Medical Association requests hospitals and physicians to cooperate with it in this important step, by seeing that bills for hospital and medical services are clearly distinguished; the latter should bear the name of the physician rendering the service to indicate clearly that the charge is for medical service.

The reference committee did not mention in its report to the House that universal conformance with the provisions of the Skinner resolution would likely achieve the desirable objectives of the Kinney resolution, but asked that the latter be referred to the Board of Trustees for study as to the "feasibility of action requested and as to ways and means of accomplishing the desired results." The House of Delegates accepted the recommendation and failed to adopt the resolution as introduced.

In its report to the House of Delegates, the Board of Trustees explained its failure to attempt a clarification of the issues referred to in the first section of the Skinner resolution by asking for time for further study by the Bureau of Medical Economics. The following statement appeared in a supplemental report presented by the Board:

The Board of Trustees has had meetings previously with hospital associations, and at least one of these hospital associations has announced plans at variance with principles set forth by the House of Delegates.

The Board has already considered this matter as a committee of the whole, and, in view of the divergent views concerning hospital plans, felt that nothing would be gained by further conferences with hospital associations until more information is available through the Bureau of Medical Economics. Such studies and compilations are in active progress, but, owing to inevitable dislocation due to the war and to constant changes in plans for hospitalization, and the heavy responsibilities laid on the Bureau of Medical Economics by the war effort, these studies have not been completed in spite of the employment of additional help. The Board would suggest that opportunity be given for further study based on the studies by the Bureau of Medical Economics.

Another resolution of particular interest to radiologists was introduced by Dr. Dwight L. Wilbur, delegate from California. It called attention to the existence of commercial laboratories which ad-

vertise to the public and which frequently give rebates to referring physicians and declared it unethical for physicians to refer patients to such concerns. The reference committee to which it was referred expressed its serious concern over the situation described and presented the following substitute resolution, which was adopted by the House:

Whereas, it has been brought to the attention of the House of Delegates that the unscrupulous practice of rebates to physicians is being engaged in by various commercial organizations, laboratories, supply houses and in some professional relationships between certain physicians; and

Whereas, all such practices are clearly in violation of the Principles of Medical Ethics; therefore be it

Resolved, that the House of Delegates of the American Medical Association express stern disapproval of the practice by any of the members of its component societies of referring patients to commercial organizations, laboratories or other physicians who advertise to the public and others than the medical profession, who employ so-called steerers or cappers or who pay, or offer to pay, rebates or commissions in any guise whatsoever, or who in any other manner violate the Principles of Medical Ethics of the American Medical Association; and be it further

Resolved, that any member violating these resolutions be subject to such disciplinary action as is deemed advisable by the county society in which such physician holds membership; and be it further

Resolved, that the Secretary of the American Medical Association be instructed to send a copy of these resolutions to each state and county society accompanied by a letter to the secretary of each, setting forth that all such unethical practices are disreputable and unscrupulous and, if not controlled, may soon besmirch the reputation of the entire medical profession.

The California delegation had been instructed to introduce the resolution by the California Medical Association following an investigation by one of its committees which revealed, among other things, that several large commercial x-ray laboratories were offering rebates to physicians who patronized them. The American Medical Association, by its adoption of the resolution, encourages county medical societies to discipline members who are guilty of participating in such practices.

The House of Delegates disapproved of a resolution introduced by New York requesting that legislation be sought to amend the Social Security Act so that persons rendering medical care to recipients-of-aid from any governmental agency may be paid directly by that agency instead of the benefits being paid in cash to the recipient. Modifying previous declarations of principle which demand that medical insurance benefits be paid in cash to the patient, the House adopted a resolution approving medical service plans which provided benefits in kind, *i.e.*, service instead of cash, "when sponsored by a constituent state medical association or a component county medical society." This leaves unchanged those principles previously adopted by the American Medical Association prohibiting the inclusion of any medical service among the benefits offered in hospital service plans.

A proposal by the Judicial Council of the American Medical Association that section delegates be deprived of their vote in the House was approved by the Reference Committee on Sections and Section Work, which will submit an amendment to the Constitution at the next annual session. The reason for the proposal is not clear. Certainly the Section on Radiology and all radiologists would be materially affected if the present excellent work of their elected delegate was interfered with in any manner. It is likely that other sections representing the specialties will feel likewise. That the proponents of the amendment are themselves somewhat obfuscated in their aims is indicated by their use of the term "*ex officio* delegates without the right to vote" in describing the status of section delegates in the proposed amendment. By parliamentary law and legal usage "*ex officio*" delegates are delegates by virtue of some office they hold and are entitled to full voting privileges, the same as any other delegate. A delegate elected by a section would not be an "*ex officio*" delegate, but a delegate. Whether these delegates are to be deprived of their vote will apparently be decided by the House at the time of its next annual session.

ANNOUNCEMENTS AND BOOK REVIEWS

AMERICAN COLLEGE OF RADIOLOGY

Dr. B. R. Kirklin, Rochester, Minnesota, was elected President of the American College of Radiology at its Annual Meeting in Atlantic City on June 10, 1942. Dr. E. P. Pendergrass, Philadelphia, was elected Vice-President, and Dr. Hollis E. Potter, Chicago, was re-elected Treasurer. Dr. J. C. Dickinson, Tampa, and Dr. W. Walter Wasson, Denver, were elected to four-year terms on the Board of Chancellors. The following representatives of the national scientific societies were re-elected to the Board of Chancellors: Radiological Society of North America, L. Henry Garland; American Roentgen Ray Society, J. C. Dickinson; American Radium Society, F. W. O'Brien.

New officers were inducted at the annual banquet on the evening of June 10, at the Chalfonte-Haddon Hall, at which time Dr. W. Edward Chamberlain delivered the annual presidential address. The College was also addressed by Col. Sam Seeley, of the Procurement and Assignment Service.

The Board of Chancellors of the College and Teachers of Clinical Radiology will hold their Annual Congress in Chicago in February of 1943. The next Annual Meeting is scheduled for San Francisco, at the time of the American Medical Association meeting.

AMERICAN RADIUM SOCIETY

The recently elected officers of the American Radium Society, for 1942–43, are as follows: President, William E. Costolow, M.D., Los Angeles; President-Elect, Charles L. Martin, M.D., Dallas; 1st Vice-President, Frank E. Adair, M.D., New York; 2d Vice-President, Eugene Pendergrass, M.D., Philadelphia; Secretary, A. N. Arneson, M.D., St. Louis; Treasurer, Leland R. Cowan, M.D., Salt Lake City.

Lawrence A. Pomeroy, M.D., Cleveland, is Chairman of the Executive Committee; Charles L. Martin, M.D., Dallas, of the Scientific Program Committee; Edward H. Skinner, M.D., Kansas City, Mo., of the Publication Committee; Edith H. Quimby, D.Sc., New York, of the Research and Standardization Committee; Ernst A. Pohle, M.D., Madison, Wis., of the Education and Publicity Committee; Douglas Quick, M.B., New York, of the Janeway Lecture Committee.

Representatives on the American Board of Radiology are Douglas Quick, M.B., New York; B. P. Widmann, M.D., Philadelphia; Frederick W. O'Brien, M.D., Boston.

AMERICAN ROENTGEN RAY SOCIETY

Since Haddon Hall, which had been selected for the 1942 meeting of the American Roentgen Ray Society, has been taken over by the Government, the Executive Council has changed the place of meeting to the Palmer House, Chicago, and the time to Sept. 15 to 18, inclusive.

ERRATUM

RADIOLOGY regrets a most unfortunate error occurring throughout the Symposium on Fungous Infections published in the June issue. The word *coccidiosis*, which properly refers to an infestation by the animal parasite *Coccidia*, is there repeatedly used to indicate the fungous infection *coccidioidomycosis*. Corrections should be made in the following papers:

Smith, C. E.: page 644, col. 1, line 37; col. 2, line 35.

Carter, R. A.: page 654, col. 1, last line.

Merchant, A. K.: page 662, col. 1, line 5.

Benninghoven, C. D., and Miller, E. R.: p. 665, legend of Figures 4 and 6.

Discussion: page 666, footnote; page 667, col. 1, lines 21 and 35; col. 2, lines 32 and 46; page 668, col. 2, line 25.

A correction should also be made in the index, p. 757.

FIFTY YEARS OF SERVICE

The long and outstanding service of Dr. James Madison Martin to the science of radiology was recognized by his fellow members of the Texas Radiological Society on June 5, 1942. At that time, pursuant to a resolution adopted at the Annual Meeting of the Society, Dr. Martin was presented with a bronze plaque bearing the signature of the members and reading as follows:

A Tribute to
James Madison Martin, M.D.
Dean of Texas Radiologists

"To commemorate 50 years of valuable pioneering service to the Science of Medicine as a whole and to Radiology in Texas in particular, this award is made by the members of the Texas Radiological Society whose signatures are herewith appended. May this plaque forever remind him of our high esteem and appreciation."

The presentation was made by Major Glenn D. Carlson of Fort Sam Houston, on behalf of the Society.

CINCINNATI RADIOLOGICAL SOCIETY

At the meeting of the Cincinnati Radiological Society, held on May 19, the following officers were elected for 1942–1943: President, Dr. Ellis R. Bader; Secretary-Treasurer, Dr. Samuel Brown.

INDIANA ROENTGEN SOCIETY

In the list of recently elected officers of the Indiana Roentgen Society, appearing in the July issue of RADIOLOGY, the name of the President, Dr. Chester Stayton, Indianapolis, was unfortunately omitted.

MIDWEST RADIOLOGISTS

The 1943 meeting of the Midwest Radiologists, originally scheduled for Chicago, has, at the invitation of the Cleveland Radiological Society, been transferred to Cleveland. Dates and details of the meeting will be announced later.

RADIOLOGICAL SOCIETY OF KANSAS CITY

At the last meeting of the Radiological Society of Kansas City, Dr. David S. Dann was elected president and Dr. Arthur B. Smith, secretary-treasurer.

SOUTH CAROLINA X-RAY SOCIETY

The South Carolina X-ray Society met in Columbia on May 21, 1942, and elected Dr. Bernard S. Kalayjian, of Roper Hospital, Charleston, president. Dr. Robert B. Taft of Charleston is the new secretary-treasurer.

SECTION ON RADIOLOGY ILLINOIS STATE MEDICAL SOCIETY

At the recent meeting of the Illinois State Medical Society Dr. Earl E. Barth succeeded to the Chairmanship of the Section on Radiology and Dr. Fay H. Squire, of Chicago, was elected secretary.

GRANT FOR STUDY OF INFANTILE PARALYSIS

Announcement has recently been made by the National Foundation for Infantile Paralysis of a five-year $300,000 grant to The Johns Hopkins University, Baltimore, for an intensive study of that disease. This grant will be used to establish and conduct the Center for the Study of Infantile Paralysis and Related Viruses at Johns Hopkins, under the direction of Dr. Kenneth F. Maxcy, professor of epidemiology in the School of Hygiene and Public Health.

In Memoriam

MAXIMILIAN J. HUBENY

1880–1942

It is with deep regret that announcement is made of the death on July 2, 1942, of Dr. Maximilian J. Hubeny, former Editor of RADIOLOGY and a past-president of the Radiological Society of North America and the American College of Radiology. An account of Dr. Hubeny's life and work will appear in the September issue of this Journal.

GEORGE FORBES

1867–1942

Dr. George Forbes of Brooklyn, New York, died on June 23, 1942. Dr. Forbes was graduated from the New York University Medical College in 1890. He was a member of the Radiological Society of North America and of the American College of Physicians.

CONSTANTINE POPOFF

1883–1942

Dr. Constantine Popoff of Haverhill, Mass., died on May 30. Doctor Popoff was born in Bulgaria and received his medical education in America, being graduated from Harvard Medical School in 1910. He was radiologist to Amesbury Hospital, Amesbury, Mass., and to Benson Hospital and the Haverhill Municipal Hospitals in Haverhill. He was a member of the New England Roentgen Ray Society and the Radiological Society of North America, and a fellow of the Massachusetts Medical Society and the American Medical Association. Doctor Popoff held the rank of lieutenant-colonel in the U. S. Army Medical Reserve and at the time of his death was awaiting orders to active service.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

AN X-RAY ATLAS OF SILICOSIS. By ARTHUR J. AMOR, M.D. (Lond.), M.Sc. (Wales), Honorary Physician, Clydach Memorial Hospital, Medical Officer, Mond Nickel Co., Ltd., Swansea. A volume of 206 pages with 72 plates. Published by the Williams & Wilkins Company, Baltimore, 1941. (Printed in Great Britain by John Wright and Sons, Ltd., Bristol.) Price $8.00.

A MANUAL OF ROENTGEN DIAGNOSIS. By KENNETH S. DAVIS, M.S., M.D., Professor of Radiology, College of Medical Evangelists, Clinical Professor of Medicine (in Radiology), University of Southern California School of Medicine, Radiologist to St. Vincent's Hospital, Los Angeles. A manual of 160 pages with 279 illustrations. Published by Cossit & Co., San Francisco, 1941.

A STUDY OF THE BLOOD IN CANCER, WITH SPECIAL REFERENCE TO THE NEEDS OF THE TUMOUR CLINIC. By O. CAMERON GRUNER, M.D. (Lond.). A monograph of 100 pages with 39 figures. Published by Renouf Publishing Company, Montreal, 1942. Price $4.00.

RADIOLOGICAL SOCIETIES OF NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate by sending information to Howard P. Doub, M.D., Editor, Henry Ford Hospital, Detroit, Mich.

UNITED STATES

Radiological Society of North America.—Secretary, D. S. Childs, M.D., 607 Medical Arts Building, Syracuse, N. Y.

American Roentgen Ray Society.—Secretary, Harold Dabney Kerr, M.D., Iowa City, Iowa.

American College of Radiology.—Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill.

Section on Radiology, American Medical Association.—Secretary, J. T. Murphy, M.D., 421 Michigan St., Toledo, Ohio.

ARKANSAS

Arkansas Radiological Society.—Secretary-Treasurer, J. S. Wilson, M.D., Monticello. Meets every three months and annually at meeting of State Medical Society.

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, Joseph D. Coate, M.D., 434 Thirtieth St., Oakland.

Los Angeles County Medical Association, Radiological Section.—Secretary, Donald R. Laing, M.D., 65 N. Madison Ave., Pasadena. Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Secretary-Treasurer, L. Henry Garland, M.D., 450 Sutter St., San Francisco. Society meets annually during annual meeting of the California Medical Association.

San Francisco Radiological Society.—Secretary, Earl R. Miller, M.D., University of California Hospital. Meets monthly on third Thursday at 7:45 P.M., for the first six months at Toland Hall (University of California Medical School); second six months at Lane Hall (Stanford University School of Medicine).

COLORADO

Denver Radiological Club.—Secretary, Edward J. Meister, M.D., 366 Metropolitan Bldg. Meetings third Friday of each month at the Denver Athletic Club.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary-Treasurer, Max Climan, M.D., 242 Trumbull St., Hartford. Meetings bimonthly, on second Thursday. Place of meeting selected by Secretary.

FLORIDA

Florida Radiological Society.—Secretary-Treasurer, Walter A. Weed, M.D., 204 Exchange Building, Orlando.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, Robert C. Pendergrass, M.D., Prather Clinic Bldg., Americus. Meetings twice annually, in November and at the annual meeting of State Medical Association.

ILLINOIS

Chicago Roentgen Society.—Secretary, Warren W. Furey, M.D., 6844 S. Oglesby Ave. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Fay H. Squire, M.D., 1753 W. Congress St., Chicago.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, Harold C. Ochsner, M.D., Methodist Hospital, Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secretary-Treasurer, Sydney E. Johnson, M.D., Louisville City Hospital, Louisville. Meeting annually in Louisville, third Saturday afternoon in April.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., North Louisiana Sanitarium, Shreveport. Meets annually at same time as State Medical Society.

Shreveport Radiological Club.—Secretary-Treasurer, W. R. Harwell, M.D. Meetings monthly on the second Wednesday, at the offices of the various members.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

Michigan Association of Roentgenologists.—Secretary-Treasurer, E. M. Shebesta, M.D., 1429 David Whitney Bldg., Detroit. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—Secretary, John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

Radiological Society of Greater Kansas City.—Secretary, Arthur B. Smith, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—Secretary, Wilbur K. Mueller, M.D., University Club Bldg. Meets on fourth Wednesday of each month except June, July, August, and September, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—Secretary, D. A. Dowell, M.D., 816 Medical Arts Bldg., Omaha. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society (Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island).—*Secretary,* Hugh F. Hare, M.D., Lahey Clinic, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, H. J. Perlberg, M.D., Trust Co. of New Jersey Bldg., Jersey City. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.—Secretary, William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, Leo Harrington, M.D., 880 Ocean Ave. Meetings held the fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Joseph S. Gianfranceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Ray Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Maurice Pomeranz, M.D., 1120 Park Ave., New York, N. Y.

Rochester Roentgen-ray Society.—Secretary, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meeting with State meeting in May, and meeting in October.

NORTH DAKOTA

North Dakota Radiological Society.—Secretary, L. A. Nash, M.D., St. John's Hospital, Fargo. Meetings by announcement.

OHIO

Ohio Radiological Society.—Secretary, J. E. McCarthy, M.D., 707 Race St., Cincinnati. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society.—Secretary-Treasurer, J. O. Newton, M.D., 13921 Terrace Road, East Cleveland. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Samuel Brown, M.D., 707 Race St. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport. The Society meets annually.

The Philadelphia Roentgen Ray Society.—Secretary, Barton R. Young, M.D., Temple University Hospital, Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

The Pittsburgh Roentgen Society.—Secretary-Treasurer, Reuben G. Alley, M.D., 4800 Friendship Ave., Pittsburgh, Pa. Meetings are held on the second Wednesday of each month at 4:30 P.M., from October to June, at the Pittsburgh Academy of Medicine, 322 N. Craig St.

ROCKY MOUNTAIN STATES

Rocky Mountain Radiological Society (North Dakota, South Dakota, Nebraska, Kansas, Texas, Wyoming, Montana, Colorado, Idaho, Utah, New Mexico).—*Secretary,* A. M. Popma, M.D., 220 North First St., Boise, Idaho.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer, Robert B. Taft, M.D., 103 Rutledge Ave., Charleston. Meeting in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—Secretary-Treasurer, L. W. Baird, M.D., Scott and White Hospital, Temple.

VIRGINIA

Virginia Radiological Society.—Secretary, Charles H. Peterson, M.D., 603 Medical Arts Bldg., Roanoke.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary-Treasurer, C. A. H. Fortier, M.D., 231 W. Wisconsin Ave., Milwaukee. Meets monthly on second Monday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russell F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

Section on Radiology, Canadian Medical Association.—Secretary, W. J. Cryderman, M.D., Medical Arts Bldg., Toronto.

Section on Radiology, Ontario Medical Association.—Secretary, W. J. Cryderman, M.D., 474 Glenlake Avenue, Toronto.

Canadian Association of Radiologists.—Honorary Secretary-Treasurer, A. D. Irvine, M.D., 540 Tegler Bldg., Edmonton, Alberta.

La Société Canadienne-Française d'Eléctrologie et de Radiologie Médicales.—General Secretary, Origène Dufresne, M.D., Institut du Radium, Montreal. Meetings are held the third Saturday of each month, generally at the Radium Institute, 4120 East Ontario Street, Montreal; sometimes, at homes of members.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meetings are held monthly.

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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Demonstration of the Basilar Artery and Its Branches with Thorotrast. Arthur B. King. Bull. Johns Hopkins Hosp. **70:** 81–89, January 1942.

In view of the absence of any unfavorable reactions in studies of the internal carotid artery with thorotrast, the author has employed this medium in a single case for demonstration of the basilar artery.

A syringe containing 10 c.c. of thorotrast was attached to an 18-gauge lumbar puncture needle bent at a right angle and this was inserted into the right vertebral artery, which had been exposed up to its origin from the subclavian artery by an incision paralleling the inner margin of the sternocleidomastoid muscle. As soon as a pulsating stream of blood returned into the syringe the artery was occluded by tightening a previously placed ligature and the thorotrast was injected as rapidly as possible. Both anteroposterior and lateral views were taken, the ligature being released between thorotrast injections.

For taking the roentgenograms a Coolidge XB 15 tube with a wide cone was used. It was placed 25 inches from the patient's head. Fifty kilovolts were delivered against the target. The exposure was half a second. A Bucky diaphragm was not used.

The right vertebral and basilar arteries were clearly demonstrated and no ill effects were observed.

If clear films are to be obtained by this procedure the vessel must be completely occluded to avoid diffusion of the thorotrast. Rapidity of action is a primary consideration. To obtain this the needle must be large, a large heavy-duty tube must be employed for taking the roentgenograms, and the work must be carried out by a group co-operating as a team.

The chief objection to thorotrast is its radioactivity and the fact of its poor excretion. It is, however, generally agreed that amounts up to 25 c.c. are probably harmless, and not more than that should be injected. For this reason, it is especially important that good films be obtained at the first attempt.

THE CHEST

Correlation of Pathology, Physical Signs, and X-Ray Appearances in the Development of Lung Cavitation. R. R. Trail. Brit. M. J. **2:** 601–605, Nov. 1, 1941.

The author presents a rather comprehensive discussion of the development and diagnosis of cavitation in the more common forms of pulmonary disease, namely, bronchiectasis, lung abscess, and tuberculosis of the acute exudative and chronic fibrotic types.

In bronchiectasis dilatation of the bronchus is the first stage of cavity formation and the progress becomes slower as the age of the patient increases. With normal respiratory action there is an accumulation of débris, which aggravates the condition, setting up a vicious cycle. Eventually a dense fibrous mass develops. X-ray findings are usually bilateral and basal, without mediastinal displacement. There is no clubbing of the fingers and only slight impairment of percussion. The film shows heavy, fluffy, linear shadows due to the increased blood supply of chronic inflammatory bronchitis. Lipiodol shows enlarged bronchi. Later comes rapid deterioration with increased fibrosis in the area of atelectasis with sepsis when perforation occurs. At this time the x-ray picture shows more irregular linear densities and possibly a shift of the mediastinum, and lipiodol shows gross sacculation. Osteoarthropathy and coarse metallic râles are now present.

In lung abscess the physical and radiological signs are entirely different throughout the development. The common site is in the more vertical right lower bronchi and the lesion is far more often peripheral than central. In place of scattered loss of translucency in the x-ray plate the shadow is confluent, ill defined in its edges, and heavy in its central zone. On physical examination there is a definite lack of movement on the affected side and the stethoscope gives a coarse pleural rub, which may be painless. In pneumonic cases coarse metallic râles are heard. There is no shift of the mediastinum. Eventually a translucency occurs toward the center and a fluid level may appear. The surrounding alveoli are filled with typical pneumonic exudate which causes induration and eventually bronchiectasis as a result of infection. The film shows a well defined cavity wall smoother than the cavities of tuberculosis and more apt to contain a fluid level. A mediastinal shift commences due to increased fibrosis and there is clubbing of the fingers.

The development of cavities in tuberculosis is, according to the author, explained by a study of the behavior of the acini with sacculation. The stethoscopic changes occur in the last phase of respiration, whereas in bronchiectasis and lung abscesses the sounds change in the early and middle phases. Films show rounded areas of loss of translucency in the subclavicular region plus many areas not unlike bronchial pneumonia. The acute exudative type of tuberculosis seldom produces a large cavity and when a cavity appears it lacks the defined inner edge of chronic abscesses and does not appear within a circumscribed cloudy area. There is no mediastinal shift and heavy circular shadows may be noted. In chronic fibrocaseous tuberculosis the earliest lesion is subapical. Sometimes a well defined annular shadow containing a fluid level appears. There is a slight but definite shift of the mediastinum toward the affected side, since fibrosis has attempted to keep pace with infiltration. Physical signs are in keeping; clubbing is present and eventually there is marked mediastinal displacement to the more affected side. The chronic cavity has a fairly wide but well defined wall with hazy distal borders, showing scattered nodules of organized and collapsed acini.

The author concludes by comparing the differentiation of these types of lung cavitation with the putting together of a jig-saw puzzle—all the parts must fit together in order to arrive at the proper conclusion.

Q. B. CORAY, M.D.

Visualization of Cavities in Post-Thoracoplasty Lungs. J. L. Leon, H. Green, and C. A. Serbst. Dis. of Chest **7:** 274–280, August 1941.

The authors accept a real fluid level as the only absolute criterion for the existence of cavity in a lung collapsed by thoracoplasty. Their patients were given codein and phenobarbital to lessen coughing and production of sputum on awakening in the morning. Early the following day fluoroscopy was done and upright and tilt films were taken at six feet. The patient then attempted to expectorate and another picture was made. This procedure was carried out from one to six times. Altogether 18 patients were examined 62 times. Eleven cases were negative on each examination (39 examinations). Even in the 7 cases where shifting fluid levels were demonstrated, positive results were obtained in only 10 out of a total of 23 examinations.

WM. H. GILLENTINE, M.D.

The Monaldi Procedure—A Progress Note. Edward Kupka. Dis. of Chest **7:** 373–377, November 1941.

The author reviews Monaldi's statistics on 330 cases of tuberculosis published at the end of 1940 and reports 17 cases of his own in which Monaldi's technic was

employed. Treatment consists in insertion of a rubber catheter through a puncture in the chest wall into the pulmonary cavity, and aspiration for about ten hours per day, at an average negative pressure of 15 to 30 c.c. of water, for two to twelve months. The author's patients have been followed for periods of fifteen to twenty-one months since the cessation of aspiration. In 3 of the 17 patients, the cavities closed; in 5 others the cavity closed with clearing of the sputum, only to reopen gradually to a slighter extent, with a return of positive sputum in 3 instances. Five patients have since received thoracoplasty. Four of the patients died, 1 of tuberculous meningitis, 1 of intestinal tuberculosis with rupture of the ileum, and 2 who were desperately ill at the time of the puncture, as a result of extension of the disease. Postmortem study in 3 of Monaldi's patients showed a clean cavity wall with a tendency toward obliteration of the draining bronchus by means of proliferating circular endobronchitis. There was evidence of epithelization of the catheter tract and alveolar dilatation in the surrounding tissues.

The author disagrees with Monaldi that continuation of the cavity with a negative sputum is to be considered as a favorable result. He recommends this procedure as a measure of symptomatic relief and in preparation for thoracoplasty. WM. H. GILLENTINE, M.D.

Relation of Chest Conditions to Sinus Disease. The Roentgenologist's Point of View. Karl Kornblum. Laryngoscope **52:** 128–142, February 1942.

The following conditions are listed as etiologically related to paranasal sinusitis: the "common cold," chronic tracheobronchitis, chronic pulmonary emphysema, bronchiectasis, bronchial asthma and hay fever.

It has been adequately demonstrated that the "common cold" is not a localized process, but one involving the entire respiratory tract—the nose and sinuses, the larynx, trachea, and bronchi. On roentgen examination the sinuses not uncommonly show an opacity of one or more groups of cells; the bronchial picture is that of a bronchitis, and though the tracheal changes are not demonstrable, the condition is generally recognized as a tracheobronchitis. While these changes tend to disappear as the symptoms of the "cold" regress, a chronic sinusitis may remain, acting as a focus of infection. The condition of the trachea and bronchi also becomes chronic, and roentgenograms of the lungs show a progressive intensification of the hilum and trunk shadows. The shadows radiate outward from the hilum into the lung parenchyma in all directions, with a tendency to be more marked in the bases. The recognition of this relationship between chronic sinusitis and chronic tracheobronchitis has given rise to the term bronchosinusitis. The designation is particularly suitable since it immediately directs attention to the dependence of the pulmonary symptoms upon chronic disease of the paranasal sinuses.

While the condition may never progress beyond a bronchosinusitis, it is followed in many instances by a chronic pulmonary emphysema or bronchiectasis, or both. The roentgen changes in emphysema are characteristic and readily recognized. The diagnosis of bronchiectasis is a more difficult problem, though in advanced cases the picture is typical. Engrafted upon the usual roentgenological manifestations of a chronic tracheobronchitis there is to be noted a predominance of heavy trunk shadows at both bases. These shadows are no longer sharp and clean cut but have become hazy and ill defined. Small patches of increased density may stud the basilar portions of the lungs. When these become so numerous and so large as to merge, there results a more or less homogeneous density, through which the heavy trunk shadows may be but dimly visible. Injection of an opaque oil may be required to establish a diagnosis in early cases. Bronchiectasis resulting from a chronic sinusitis is almost invariably bilateral and is limited to or is predominant in the bases of the lungs. When a bronchiectasis is unilateral and localized to one lobe, especially an upper lobe, the etiology is usually not to be found in the sinuses. If a sinusitis is present it is more likely to be the result than the cause of the pulmonary disease.

Victims of hay fever and asthma not infrequently exhibit chronic infection of the nose and sinuses and a chronic tracheobronchitis. A long history of chronic sinusitis without roentgenographic evidence of pathology is suggestive of an allergic basis.

Tuberculous Stenosis of the Major Bronchi. Wm. M. Tuttle, E. J. O'Brien, J. C. Day, and F. J. Phillips. J. Thoracic Surg. **11:** 299–307, February 1942.

This study deals only with bronchial obstruction which has been caused by intrinsic stenosis as a result of ulcerative tuberculous tracheobronchitis. Ninety-two cases were studied and all had been followed for more than one year. The stenoses were classified as either ulcerous or fibrous in type. There were 69 of the former and 23 of the latter. The fibrous lesions were treated only by dilatation in order to make room for evacuation of secretions distal to the obstruction. The ulcerous lesions received topical applications of 30 per cent silver nitrate at intervals of two or three weeks, and healing occurred in 48 of the 69 cases thus treated. At the time of the report 23 of the 69 patients had died, death being most commonly due to post-stenotic suppuration. A patient with a healed stenotic lesion appears to face great uncertainty because of pulmonary suppuration distal to the stenosis. In such cases chemotherapy has failed.

Pneumothorax is usually unsatisfactory in the presence of bronchial stenosis, especially if the degree of narrowing is marked. Empyema is a common complication. Forty-seven patients in the present series had pneumothorax to control the pulmonary suppuration and in only 12 instances was the procedure considered satisfactory; 13 patients are dead. Thoracoplasty gives better results. This procedure was employed in 34 patients, and of this group only 5 are dead. Pneumonectomy has not proved satisfactory up to the present time. Twenty-two cases of pneumonectomy from the literature and other discussions were reviewed. Ten of the patients were dead and only 3 were considered to be well.

Tuberculous stenosis of the major bronchi is a serious complication. Of the entire group of 92 patients, 32.6 per cent are dead. A remaining 33 per cent are unstable. About one-third of the cases have a chance of becoming arrested. Routine bronchoscopy is advised before all initial pneumothorax injections and before thoracoplasty. HAROLD O. PETERSON, M.D.

Bronchitis Plastica. Sandro Seiler. Schweiz. med. Wchnschr. **72:** 86–90, Jan. 24, 1942.

Bronchitis plastica is an extremely rare disease characterized by the coughing up of bronchial casts. Only about 100 examples are described in the literature. One case, treated by pneumothorax with good results, is here reported. The condition may be acute or chronic, and occurs mostly between the tenth and thirtieth years, generally in women. The acute form begins suddenly with cough, dyspnea, and typical sputum. Generally there is a high fever. Splenic enlargement and pneumococci in the sputum are usual. A limited portion of a lung is decreased in volume and symptoms of atelectasis develop, although physical signs may be absent. Massive atelectasis may occur. The course is from one day to a few weeks; the mortality is 25 to 50 per cent.

The chronic forms shows recurring attacks of cough, dyspnea, and expectoration of casts. There may be no physical signs or these may be limited to a slight respiratory infection. Occasionally fever, malaise, and hemop-

tysis are noted. After coughing up the casts, most patients experience a rapid improvement. The prognosis for life is good, but the disease tends to recur. There is no specific therapy.

The etiology of bronchitis plastica is unknown. The casts may be white or bloody, at times with a central lumen; they are lamellated and contain fatty substances, eosinophils, neutrophils. Charcot-Leyden crystals, microorganisms, blood and metabolic products, heart failure cells, and corpora amylacea-like bodies. They may be either fibrinous or mucinous in character. At autopsy the bronchial mucosa is reddened and loose, but the epithelium is generally retained.

The author believes that collapse therapy by artificial pneumothorax is the best treatment, as shown by analysis of his case. LEWIS G. JACOBS, M.D.

Lung Injury Due to the Detonation of High Explosive. James D. King and George M. Curtis. Surg., Gynec. & Obst. **74:** 53–62, January 1942.

The authors review the recent clinical and experimental studies that have been made on the effects of detonation of high explosives on human beings and animals. Particular attention is given the pulmonary system. Wartime "blast" injuries are compared with "similar" peacetime injuries, largely by means of numerous references to the literature. An epitome of the physics and chemistry of explosion or blast" is presented.

The symptoms of blast injury of the lungs vary from slight dyspnea to complete cessation of respiration, depending on the degree of injury. Cough and hemoptysis are common. Varying degrees of shock occur.

It is emphasized that physical examination may not reveal evidence of external injury to the thorax. Injuries elsewhere in the body must not be allowed to overshadow possible lung damage. The presence of blood in the nose or mouth and of bloody sputum is of considerable importance.

The authors state that postmortem examination always reveals extensive hemorrhagic lesions in the lungs and all cases show general pulmonary congestion. No details of the characteristic roentgen findings are given.

References to the papers cited in the text are not appended, but a complete bibliography is furnished with the reprints. IVAN J. MILLER, M.D.

Air-Raid Injuries of the Chest. Thomas F. Rose. M. J. Australia **2:** 465–468, Oct. 25, 1941.

The author states that chest injuries form a small percentage of the total air-raid casualties reaching the surgeon's hands, since most of these wounds are fatal. Injury may be due to shrapnel from anti-aircraft shells, machine gun bullets from low-flying aircraft, or the bomb itself. An exploding bomb produces its effect by fragments of the bomb casting, by the blast or suction wave, or indirectly through the destruction of buildings.

Principles of treatment seem simple. If the chest wall has been rendered flexible by multiple rib injuries, it should be made rigid by strapping. In tension pneumothorax affecting respiration, the excess air should be removed. Débridement should not only include the chest wall, but also blood clots, etc., within the pleural cavity. Openings in the pleural space hould be closed. Drainage should be instituted in almost every case, because of the primary contamination of the cavity and the necessity of further drainage of fluid; also, because of possible contamination from ruptured bronchi or injured lung and to facilitate treatment of infections when they occur.

The author recommends that all patients near an exploded bomb be treated prophylactically, with bed rest in the hospital, for lung blast. This may not appear clinically for twelve to twenty-four hours and x-ray facilities are not widely available. Gaping wounds are packed in an effort to obtain adhesions between the visceral and parietal pleura, after which skin grafting may cover this defect of the chest wall. Sulphapyridine is used to control infection.

WM. H. GILLENTINE, M.D.

Malignant Thymoma. Clinical-Pathological Study of Eight Cases. C. Alexander Hellwig. Surg. Gynec. & Obst. **73:** 851–863, December 1941.

The author groups the 8 thymic tumors upon which his report is based as follows: lymphosarcomas, 4; lymphoid leukosarcomatosis, 1; Hodgkin's disease, 2; carcinoma 1. These he compares with cases recorded in the literature.

Autopsy was done in 2 of the cases of lymphosarcoma, the case of leukosarcomatosis, one of the cases of Hodgkin's disease, and the case of carcinoma. All these showed invasion of the pericardium and 3 of the heart muscle as well. The pleura was invaded by the 2 lymphosarcomas and by the carcinoma, the invasion being diffuse or in the form of circumscribed nodules. In all 5 cases the large bronchi were buried in tumor tissue but in no case was the bronchial mucosa invaded.

Four of the patients died within five to thirteen weeks after the first pressure symptoms were noticed, though the anatomical findings pointed to a much longer existence of the growth. This absence of early symptoms, with a rapid course after evidences of pressure become apparent, is characteristic of thymic tumors and makes early diagnosis difficult. Differentiation of malignant thymomas and benign mediastinal growths is, however, imperative, since the tumors of lymphoid origin may be controlled, at least temporarily, by irradiation, while carcinoma is hopeless from the onset. Certain distinguishing roentgen features have been mentioned by Lenk (Die Röntgendiagnostik der intrathorakalen Tumoren und ihre Differentialdiagnose, Wien, Julius Springer, 1929). According to him in lymphosarcoma the x-ray shadow has an irregular, hazy contour and the mediastinal organs are usually not displaced. In Hodgkin's disease the contour is more clear cut and there is less evidence of infiltrative growth. In carcinoma the shadow is broader than long and tracheal displacement is more frequent than in the other types. These findings, however, are not conclusive. Biopsy and microscopic study of the tumor tissue are essential for an accurate diagnosis.

Arteriosclerotic Aneurysms and Senile Ectasia of the Thoracic Aorta. Marshall de G. Ruffin, Benjamin Castleman, and Paul D. White. Am. Heart J. **22:** 458–468, October 1941.

In 9,600 postmortem examinations done in the past forty-five years at the Massachusetts General Hospital, 116 cases of aneurysms of all sorts involving the thoracic and abdominal aorta were found, *i.e.*, 1.2 per cent of the total necropsies. Of this group 17 were cases of true and dissecting aneurysms with medionecrosis aortae cystica and 13 were cases with small dissections in and about atherosclerotic plaques. These are not discussed in the present paper. Of the remaining aneurysms 86 involved the aorta, 66 being in the thorax. Sixty of this latter number were syphilitic and 3 definitely arteriosclerotic; in 3 cases there was marked dilatation of the ascending aorta without arteriosclerosis, a condition the authors term "senile ectasia." Of the 20 abdominal aortic aneurysms, 3 were syphilitic and the other 17 arteriosclerotic. All of the former and a third of the latter ruptured. The average age of death in the entire syphilitic group of 63 cases was 46.4 and in the arteriosclerotic and senile ectasia group of 23 cases, 72.7 years.

Arteriosclerotic aneurysms may be suspected where the combination of old age, female sex, and a negative serologic reaction occurs. Some generalized dilatation

of the ascending aorta with advancing age must be pointed out as not an uncommon finding.

WM. H. GILLENTINE, M.D.

Coarctation of the Aorta in Children: Syndrome of Constriction of Isthmus of Aorta, with Involvement of Origin of Left Subclavian Artery. Sidney B. Schwartz and David Greene. Am. Heart J. **23:** 99–113, January 1942.

The clinical signs associated with coarctation of the aorta which involved the origin of the left subclavian artery were studied in two children. Each showed an asymmetrical development of the upper half of the body; the right half of the chest was larger than the left, and the right upper arm was longer and larger in circumference than the left. In neither were pulsations present in the left axillary, brachial, and radial arteries. At times pulsation of the left carotid artery was diminished. The blood pressure was obtainable in the right arm only. It was elevated in one child and within normal limits in the other. In one child, with aortic insufficiency, a roentgenogram of the chest revealed sulci and grooves in the caudad portions of the posterior sections of the ribs on the right side only. In the second child, who had a widely patent ductus arteriosus, there was no collateral circulation. The pulsations of the abdominal and femoral vessels were absent, or retarded, or diminished in volume, and this was confirmed by oscillographic readings.

In the presence of such abnormalities, coarctation of the aorta, with involvement of the orifice of the left subclavian artery, should be easily suspected.

The authors include a table of the reported observations on coarctation of the aorta with subclavian artery involvement (10 cases).

WM. H. GILLENTINE, M.D.

Body Section Radiography in the Diagnosis of Aortic Aneurysms and Mediastinal Tumors. Wendell G. Scott, Sherwood Moore, and Thomas G. Russell. Southern M. J. **34:** 343–351, April 1941.

Several cases are reported, with photographs, showing the information which can be obtained from body-section radiography in suspected mediastinal pathology in addition to that furnished by conventional roentgenograms. Body section radiography outlines the aorta and other mediastinal structures with unusual clarity, and demonstrates more adequately the relationship of abnormal shadows to the aorta.

The heart and aorta stand out in relief, as if injected with opaque material, thereby rendering more clearly visible the pathological changes suspected from roentgenograms made in the usual manner. The left anterior oblique position is most informative. An unusual and interesting case of aneurysm of the ductus arteriosus proved by surgery is included.

JOHN M. MILES, M.D.

THE GASTRO-INTESTINAL TRACT

Roentgen Diagnosis of Early Ulcerating Stomach Cancer and Malignant Degeneration of Simple Stomach Ulcer in the Early Stage. E. Walder. Schweiz. med. Wchnschr. **71:** 1585–1594, Dec. 20, 1941.

On the basis of three cases it is demonstrated that in early ulcerating carcinoma of the stomach, on the one hand, and in ulcer undergoing carcinomatous change, on the other, roentgenologically demonstrable bumpy or knobby shadows may appear at the edges of the niche and grow to the size of an apple seed or pine nut. These are confined to one of a few locations or to a greater or lesser sector of the ulcer wall. In their roentgenologic aspect these ulcers show almost without exception the signs of benignity. The bumps or knobs are to be found only at the point at which cancer as such is proved, even though the cancer is so small that the ulcer seems roentgenologically benign or inconclusively malignant. This picture is never observed in benign ulcers, so that we must think of malignancy whenever it is seen in the vicinity of a niche. Further observation will show whether this can be accepted as a certain sign of carcinomatous ulcer.

It is shown that a rosary-like arrangement of such knobby shadows in a limited area which is subjected to compression during a barium examination can lead to an appearance resembling an *en face* niche, which in contrast to a true niche cannot be shown in profile.

On the basis of a case of callous penetrating ulcer (non-malignant) with cascade or beginning hour-glass stomach, it is shown that the picture of rigidity and irregularity of the wall can arise without carcinomatous infiltration solely as a result of the combination of projection of shadows in different planes and limited compression of neighboring structures (pseudo-rigidity and pseudo-infiltration).

LEWIS G. JACOBS, M.D.

Hiatus Hernia of the Stomach: Incidence, Symptoms, and Medical Management in 1,220 Gastro-Intestinal Cases. Moise D. Levy and L. B. Duggan. South. M. J. **34:** 351–357, April 1941.

On the basis of reported gastro-intestinal studies the incidence of esophageal hiatus hernia of the stomach appears to be from 2 to 3 per cent of all cases examined roentgenographically. The authors found 26 examples (2.1 per cent) in a series of 1,220 examinations. The diagnosis is best made from roentgenograms of the barium-filled stomach taken in the prone right anterior oblique position. The hernia, as a rule, disappears in the erect position.

Symptoms may be absent; if present, they may be cardiac, respiratory, gastro-intestinal, or constitutional. Vague epigastric discomfort following meals and aggravated when the patient assumes the recumbent position is common. Palpitation of the heart, dyspnea, and anginoid pains may occur. Secondary anemia of the hypochromic type is a frequent finding, and there may be bleeding into the gastro- ntestinal tract.

Surgery is necessary in severe cases, but symptomatic medical treatment is satisfactory in most. Since a spastic constipation is nearly always present, simple intestinal lubricants and antispasmodic drugs are given. The authors have found it helpful to direct the patient's attention toward the treatment of the associated conditions rather than toward the actual physical defect, thus minimizing the possibility of a neurosis. A bland high-vitamin diet is given, with four to six small feedings daily, and the patients are advised not to lie down immediately after meals. Tight abdominal bands are to be avoided. Iron and transfusions are given for anemia.

The authors tabulate their 26 cases and give reports of some of them, with roentgenograms.

JOHN M. MILES, M.D.

Radiological Findings in the Terminal Ileum and the Proximal Colon: A Twenty-Five Year Post-Operative Retrospect. L. J. Carter. Canadian M. A. J. **46:** 151–155, February 1942.

The author reviews 1,000 consecutive operations upon the terminal ileum and proximal colon performed at the Bigelow Clinic (Brandon, Manitoba). Among these were 12 cases of carcinoma of the cecum and 6 of tuberculosis of the ileocecal region. Thirty-nine cases of conditions not related but proximal to the terminal ileum and ascending colon, *i.e.*, tubular and ovarian disease and retroverted uterus, are included. The author believes that in the remaining 943 cases the principal cause of trouble was the presence of pathological bands or membranes extending from the parietal

peritoneum across the terminal ileum, the appendix or its mesentery, the cecum, and ascending colon. Emphasis is placed on the importance of these bands and the relief obtained when they are severed. An appeal is also made to roentgenologists to pay especial attention to their occurrence. The author outlines his technic of examination. M. L. CONNELLY, M.D.

Case of Fixed Congenital Right-Sided Sigmoid. E. Ledergerber. Schweiz. med. Wchnschr. **72:** 64–65, Jan. 17, 1942.

A five-year-old boy was operated on for appendicitis. The cecum lay under the liver, and the sigmoid made a wide loop so as to occupy the right lower quadrant. The patient's mother had a similar wide loop in the sigmoid, but no cecal displacement. The father and one brother were normal in this respect.

LEWIS G. JACOBS, M.D.

Foreign-Body Eaters. Max Tschamper. Schweiz. med. Wchnschr. **71:** 1607–1608, Dec. 27, 1941.

On the basis of 9 cases reported from the Zurich Ear Clinic and the Polyclinic the author believes that people who ingest foreign bodies (exclusive of accidental ingestions) have more or less outspoken mental aberrations. Foreign-body eating is only a symptom which arises in various types of mental disturbance. Especially noteworthy were the splitting of the personality and the return to an infantile or more primitive state.

LEWIS G. JACOBS, M.D.

THE BILIARY TRACT

Significance of Calcification in the Gallbladder. S. Paul Perry and James W. J. Carpender. Pennsylvania M. J. **45:** 477–481, February 1942.

It is the belief of the author that calcification within the gallbladder occurs only in the presence of cystic duct obstruction. A normal gallbladder is radiotranslucent, and when one is filled with milk of calcium bile or stones it must be assumed that the "cystic duct is or at some time in the past has been obstructed."

Ten cases seen over a period of four years are recorded. JOSEPH T. DANZER, M.D.

THE PERITONEUM

Pneumoperitoneum after Laparotomy. R. Imbach. Schweiz. med. Wchnschr. **71:** 1574–1575, Dec. 20, 1941.

During laparotomy air enters the peritoneal cavity and remains as a greater or lesser air mass after closure. This air is clinically recognized by a partial or complete loss of liver dullness and roentgenologically by a radiolucency between the liver and the diaphragm. Through pressure changes in the abdomen the air produces stimuli on the sensory receptors in the diaphragm and may cause subjective symptoms, such as shoulder pain, stabbing pains in the chest, or substernal fullness. These harmless manifestations may be confused with lung infarct, especially when a slight dyspnea is present from the elevation of the diaphragm.

LEWIS G. JACOBS, M.D.

THE SKELETAL SYSTEM

Recurrent Fracture. Wm. A. Evans. Surg., Gynec. & Obst. **74:** 204–219, Feb. 1, 1942.

The author presents a series of 16 cases of recurrent fractures in various bones. The cases are divided for purposes of discussion into two groups. In one there were general and local pathological bone conditions predisposing to recurrence; in the other the recurrent fracture occurred after the first fracture had healed in an apparently normal fashion and presented a normal roentgen appearance.

It is pointed out in the discussion that recurrent fractures in areas of pathological bone structure are easily understood, but 8 of the cases presented were in children, involving the mid-portions of the shafts of the radius and ulna with no recognizable complicating pathological process. In these 8 cases, however, the author believes that the second fracture line shows a peculiar configuration suggesting abnormal fragility of the bone and that healing of the first fracture failed to restore the bone to its original strength. These second fracture lines resemble those seen in osteogenesis imperfecta, rickets, and the condition known as "insufficiency fracture."

The author discusses possible reasons for the apparent fragility of some healed fractures and cites points in his series which have a bearing on this matter. In 4 of the cases the fractures were far from the usual position of the nutrient foramen, but the possibility is suggested that in the shaft, where the cortex and medulla are sharply differentiated, the blood vessels and nerves may be more seriously injured than in the cancellous portions without involvement of the foramen.

Many of the children in the author's series showed constitutional peculiarities. Some tended to be undernourished. Several were below the general average in weight, and many of them exhibited thin, bluish sclerae and "hyperflexibility of the ligaments suggesting a mild form of osteogenesis imperfecta." The author found that 2 of his patients having abnormal fragility of the primary fracture site suffered upper respiratory infections during healing of the fracture.

There was clinical evidence of healing of the first fracture in all 8 cases and x-ray evidence in some of them. Acute trauma attended the second fractures and roentgenologically they sometimes resembled fractures such as march foot (excess callus due to early movement of contiguous fragments).

The author believes it is desirable for children who have had fractures of the shafts of radius and ulna to take particular care to avoid a second injury to the part even after healing seems complete and that the general nutritional state of the patient be improved if possible. IVAN J. MILLER, M.D.

Critical Survey of Ten Years' Experience with Fractures of the Neck of the Femur. Mather Cleveland. Surg., Gynec. & Obst. **74:** 529–540, Feb. 16, 1942.

The author analyzes 110 fractures of the femoral neck treated during the past ten years. The first 50 cases were treated by manipulation and application of a plaster cast or traction; another group of cases underwent open operation and fixation; in the later years closed reduction and internal fixation by means of a nail have been employed.

The author finds that closed reduction and internal fixation gave good results and required a much shorter period of hospitalization than the other methods. With open operation and internal fixation there was very little improvement of the end-result over manipulation and application of a cast. Circulatory disturbances of the head of the femur took place in the author's cases within the first year if they occurred at all.

Two instances are cited of inadequate reduction of the fractures of the femoral neck although they were manipulated with the aid of the fluoroscope. In the author's opinion the fluoroscope has no useful function in the reduction of these fractures. The importance of x-ray films of good technical quality in the anteroposterior and lateral projections during operation is emphasized.

[The author has not classified his femoral neck fractures in the manner suggested by Garland and Hill (Radiology **33:** 421, 1939) and the value of his conclusion in the comparative groups is therefore somewhat vitiated.—I. J. M.] IVAN J. MILLER, M.D.

Materials for Internal Fixation of Intracapsular Fracture of the Neck of the Femur. Edward L. Compere, George Wallace, and John Lee. Arch. Surg. **44:** 327–337, February 1942.

The authors tested on anatomical specimens the mechanical forces necessary to produce primary fracture of the femoral neck, to disrupt by shearing force the pinned fragments, and to avulse them. Tests were made after fixation with threaded wires, Steinmann pins, and Smith-Petersen nails. Threaded steel wires inserted horizontally (not in the axis of the neck) had the best holding powers in all types of test. They are also superior anatomically, since they produce less disruption of the cancellous bone and of the blood supply. The use of small nuts tightened against the femoral cortex laterally increases the efficiency of immobilization. LEWIS G. JACOBS, M.D.

Car Window Elbows. Howard B. Shorbe. Southern M. J. **34:** 372–376, April 1941.

Thirty-two cases of injury caused by riding with the elbow on an automobile window are reviewed. The elbows were struck by passing objects with resultant fractures, generally of a severe nature. Fractures of the metacarpals were frequently found as well, apparently due to the hand striking the side of the car. Nerve and other soft tissue injuries were frequent complications.

The treatment is discussed and the importance of early attention is stressed. Suturing of several blood vessels and nerves is often necessary. Tetanus and gas gangrene antitoxin is administered. Sulfanilamide crystals are placed in the wound. The treatment of the fracture varies with the degree of injury and bones involved. JOHN M. MILES, M.D.

Coccidioidal Arthritis. Report of a Case in Which the Ankles Were Involved and the Condition Was Unaffected by Sulfanilamide and Roentgen Therapy. Edward F. Rosenberg, Malcolm B. Dockerty, and Henry W. Meyerding. Arch. Int. Med. **69:** 238–250, February 1942; correction **69:** 717, April 1942.

The joints may be involved in either the acute benign phase of coccidioidomycosis (valley fever) or in the more serious chronic granulomatous phase. In the former, while the joint involvement may be distressingly painful, it is of no serious significance, as it subsides completely. In the latter it may be the forerunner of disseminated infection which will prove fatal.

About a third of the patients with valley fever have signs of acute arthritis, usually appearing simultaneously with erythema nodosum. The joints are tender to pressure, painful on motion, and may be slightly swollen. Effusion and suppuration have never been observed. The salicylates are indicated for relief of the pain.

Joint involvement is fairly frequent in the chronic granulomatous stage of coccidioidomycosis. In a report of 256 cases (Special Bulletin 57, State of California Department of Public Health, June 1931) it was recorded in 79. The joints are swollen and red and nodular lesions may develop in the overlying skin, subsequently ulcerating and discharging pus containing Coccidioides immitis. Roentgenographically the joint lesions may resemble those of tuberculous arthritis. Early lesions are characterized by regions of destruction in articular surfaces, often with evidence of swelling of overlying soft tissues; cartilage may be destroyed and joint spaces narrowed; there is little tendency toward production of bone. In later lesions there may be complete disappearance of joint spaces, more extensive zones of destruction in articular surfaces, and, in some instances, ankylosis. But whereas tuberculosis appears often to attack joints directly, coccidioidal granuloma usually does so by extension from adjacent bone lesions, and the latter involvement more often affects multiple joints.

A case of cocc dioidal granuloma with bilateral ankle involvement is here recorded. The patient had previously lived and worked in the San Joaquin Valley, California, which is the main reservoir of the infection. The ankles had been painful and swollen for a year and weight-bearing had become intolerable. Roentgenograms showed swelling of the soft tissue with flecks of calcification in the swollen regions. Some erosion of the joint surfaces was seen. A biopsy led to the correct diagnosis. Sulfanilamide and roentgen therapy were tried but the patient was discharged unimproved.

The authors include a table presenting the chief laboratory and histologic points in the differential diagnosis of coccidioidal granuloma, blastomycosis, and torulosis. References to the literature are given and illustrative roentgenograms and photomicrographs are reproduced.

Differential Diagnosis of Carcinoma of the Prostate with Skeletal Metastases and Osteitis Deformans (Paget's Disease of Bone). John K. deVries. J. Urol. **46:** 981–996, November 1941.

Without the aid of roentgenology, the differential diagnosis of carcinoma of the prostate with skeletal metastases and osteitis deformans (Paget's disease of bone) is almost impossible. Age, history, and symptomatology may be similar. Digital examination is reliable only on a positive diagnosis of carcinoma and negative examination in cases of Paget's disease. Cystoscopy and cystourethrograms are of value as corroborative clinical evidence. Aspiration biopsy is reliable only when a positive finding of cancer is made. Phosphatase activity determination has definite diagnostic value.

Roentgenology offers two classes of evidence upon which to make the differential diagnosis. First, the distribution of the lesions; second, the type of bony changes produced. In so far as distribution is concerned, although the spine, pelvis, and long bones may be affected by either condition, a skull lesion will most likely be Paget's disease, a rib lesion most likely carcinoma.

As recorded by the x-ray, the following changes occur in *Paget's disease.* In the *pelvis* the bones are thickened, and coarse trabeculations replace the normal bony architecture. In the *femur* there is cortical thickening, with a corresponding decrease in the marrow space. Bowing is present. In the *skull,* the tables show marked thickening with large patchy areas of increased density.

In *metastatic bone lesions from prostatic carcinoma,* the appearances as recorded by the x-ray are as follows. In *osteoplastic metastases in the spine and pelvis* trabeculations are not visible. When the osteoplastic process is advanced, there is considerable increase in bone density, giving a mottled, spotty appearance. On close observation minute areas of decreased density may be seen surrounded by areas of increased density. This appearance probably represents minute areas of tumor cells surrounded by new bone. Actual bone expansion may take place, as pointed out by Marks, but the appearance is different from the thickening which occurs in Paget's disease. There is no bowing of the long bones in spite of extensive processes, no cortical thickening, no reduction of marrow space. *Osteolytic* lesions are characterized by areas of decreased density. In other cases, the lesions may be mixed, both osteoplastic and osteolytic areas being present at the same time.

Finally it is well to remember the possibility of both conditions occurring simultaneously in the same patient. BENJAMIN H. ORNDOFF, M.D.

Roentgenologic Changes in the Bones in Cases of Pseudohypertrophic Muscular Dystrophy. B. S. Epstein and J. L. Abramson. Arch. Neurol. & Psychiat. **46:** 868–876, November 1941.

Epstein and Abramson studied the roentgenologic changes in the bone in seven cases of pseudohypertrophic muscular dystrophy. In six, the scapulae and other long bones were involved, while in all seven the pelves were deformed. The most constant changes noted were: symmetrical diminution in the size of the scapulae, disproportionately large humeral head in relation to the small shallow glenoid fossa, slender humeral shafts with widened medullary canals and thin but not atrophic cortices, and in several instances, unusually slender femora, fibulae, radii, and ulnae. The pelvis was small in each of the patients. There was flaring of the iliac bones, prominence of the ischial spines, and marked coxa valga. The authors believe that the changes in the pelvis, aside from the coxa valga, were probably due to the many years which the patients had spent in wheel chairs as a result of their disease, for in one of their ambulatory patients, whose pelvis was of normal configuration, a coxa valga was present.

C. G. Dyke, M.D.

GENITO-URINARY TRACT

Clinicopathologic Discussion of Hyperplastic Lesions of the Urinary Tract. W. Calhoun Stirling and J. E. Ash. Southern M. J. **34:** 358–364, April 1941.

This clinical paper supplements an earlier one by the same authors (J. Urol. **45:** 342, 1941) on the pathology of proliferative lesions of the urinary tract. As stated in the earlier paper, it is not sufficient to group these cases under a single heading such as "cystitis cystica." Six types are recognized by Hinman (Hinman and Cordonnier: J. Urol. **34:** 302, 1935): pyelo-ureterocystitis cystica, granulosa, glandularis, follicularis, emphysematosa, and bullous edema. The authors add a seventh classification—"papillary hyperplasia" and report a case which they believe to be the first recorded in the literature. In this lesion the mucosa of the bladder is thrown up into blunt papillae by edema, exudate, and/or granulation tissue, and the appearance may suggest a neoplasm.

Hyperplastic or proliferative disease of the urinary tract is of interest because it is a cause of hematuria, dysuria, and frequency and because of the possibility of malignant change. Involvement of a single portion of the urinary tract other than the bladder is uncommon.

X-ray studies of a typical case of hyperplastic disease with renal involvement show dilatation of the terminal calices, narrowing of the infundibula and spherical dilatation of the kidney pelvis. Cysts in the mucosal wall may produce filling defects, dilatation, and tortuosity or constriction of the ureter. Bilateral pyeloureterograms should always be made if a cystoscopic diagnosis of cystitis cystica is verified by biopsy.

John M. Miles, M.D.

Exploration of Certain Renal Tumors. Henry G. Bugbee. J. Urol. **46:** 1–16, July 1941.

If, after complete study of all data, reasonable doubt still exists as to the diagnosis of renal tumor, surgical exploration must be done. Irradiation should be regarded as a compromise, to be instituted when excision of the kidney is not possible.

Three groups of cases are presented. In the first group, illustrated by four case reports, diagnosis was based upon minimal evidence, but the finding of cancer in a kidney of normal size and shape justified the courage and convictions of the operator. In the second group, illustrated by two cases, the presence of a tumor with symptoms and findings due only to pressure was shown to be a valid indication for operation. Large benign neoplasms were found. The third group includes large tumors with all the signs, symptoms, cystoscopic and urographic data characteristic of a renal neoplasm. In both instances in this group the tumor at first appeared inoperable but was readily removed after radiotherapy had appreciably reduced its size.

It is questionable whether irradiation should be employed routinely before or after operation. Cases should be treated individually. Arguments which might be presented as contraindicating routine roentgen therapy are the fact that in certain instances benign tumors cannot be differentiated from malignant tumors preoperatively; that often an unnecessary toxemia from the radiotherapy is imposed upon the patient, lowering his resistance; that the delay in operating may prove a serious loss to the patient, possibly giving time for metastases to develop. In reducing the size of renal tumors irradiation apparently causes a destruction of thin-walled blood vessels, with the production of hemorrhagic infarcts which may, in turn, destroy areas of tumor tissue, the effect being a partial removal of the tumor. Tumor cells, however, have always been found adjacent to such areas of tissue destruction.

Benjamin H. Orndoff, M.D.

Large Solitary Cysts of the Kidney: Types, Differential Diagnosis, and Surgical Treatment. R. Gutierrez. Arch. Surg. **44:** 279–318, February 1942; correction **44:** 598. 1942.

Gutierrez classifies renal cysts as (1) multiple minute cysts, commonly found in patients with chronic nephritis or in otherwise normal kidneys, (2) polycystic disease, and (3) large solitary serous cysts. Only cysts of this last type are under discussion in the present paper. These are subdivided into congenital and acquired types; but the author questions whether there is not some embryonic basis for all of them

Cysts may be unilocular, bilocular, or multilocular, and vary in size from "that of a walnut to that of an orange or grapefruit"; exceptionally one may occupy the entire abdominal cavity. The most common site is the lower pole of the kidney; the upper pole and the anterior wall are next most common. Cysts are not infrequent in anomalous or aplastic kidneys. They may be perinephric, pararenal, or may even be found in some neighboring organ.

A simple serous cyst may in the course of its development change in type; it may become hemorrhagic, purulent, neoplastic, calcified, or stone-bearing. Connection with the renal pelvis may be present, but the very large cysts are rarely so attached.

The cause of renal cysts is unknown. Simple localized degeneration, interstitial nephritis, and development of embryonic rests have been cited. Occlusion of both blood supply and tubules experimentally has led to cyst formation in the kidneys of rabbits. Certain extrinsic factors such as trauma and arteriosclerosis seem to have some association. It seems certain that both congenital and acquired factors operate in most cases.

Symptoms are generally absent until the cyst is large enough to produce pressure. Urinary symptoms especially develop very late. Heaviness, pain in the lumbar region or costovertebral angle, or more acute distress may be present. Gastro-intestinal symptoms may be most prominent. If the cyst compresses the urinary tract it may cause symptoms here; unexplained hematuria is not infrequent. Weakness, secondary anemia, emaciation, and general poor health are occasional complaints.

The cysts are usually unilateral and involve the cortex, although opinion differs as to whether or not they originate there. As the cyst increases in size, it hollows out for itself a bed in the parenchyma, and where it encroaches upon this, slight inflammatory changes may be present.

The cyst wall is thin, fibrous, and transparent, of a bluish or whitish color, and traversed by many vessels.

The thinness of the wall distinguishes the serous from the hemorrhagic cyst. The wall consists of the fibrous capsule of the kidney, connective tissue containing vessels and atrophic remnants of renal structures, and an inner layer of pavement or cuboidal epithelium. It may contain calcareous deposits. The cyst content is a serous or serohematic fluid whose specific gravity is from 1.002 to 1.018; the chemical composition is quite constant—water, albumin, chlorides, phosphates, sulphates, serum, globulin, fats, cholesterol crystals, and urea. Cellular elements are also found.

As the cyst grows, it forms adhesions to neighboring structures. It is usually sessile but may have a pedicle. Connection with the renal pelvis is unusual, but may result from infection or other cause, producing a corresponding alteration in the picture. Rupture into other organs may occur. Neoplasm may be found in the cyst wall.

The history and physical signs are not helpful in establishing a diagnosis. Cystoscopic findings are normal, and ureteral catheterization is useful only in the presence of obstruction. Pyelography is usually diagnostic if the cyst is large enough to produce deformity. Lower pole cysts are often the cause of a hydronephrosis which masks any deformity present in the kidney. The cyst itself can often be distinguished on properly made roentgenograms. In many instances upper pole cysts cannot be diagnosed. Renal arteriography and aspiration are occasionally helpful.

Treatment may be omitted if the cyst is small, symptomless, and does not interfere with the function of other organs. In these circumstances a close check should be kept on its progress. Otherwise surgical removal by partial nephrectomy or complete nephrectomy is indicated; rarely marsupialization may be employed. Aspiration is dangerous and ineffective.

The points made by the author are illustrated by 10 case reports and several drawings. Altogether this is an excellent article. LEWIS G. JACOBS, M.D.

Papillary Carcinoma of the Renal Pelvis. Diagnosis and Treatment. Thomas J. Kirwin. Surg., Gynec. & Obst. **73:** 759–765, December 1941.

With improvement in methods of urologic diagnosis the incidence of papillary carcinoma of the renal pelvis has shown an apparent rise. Johnson (Northwest Med. **38:** 236, 1939) stated that these tumors comprise 4.9 per cent of all tumors of the kidney. The growths are most often found at the ureteropelvic junction and for this reason early invasion of the ureter is likely to occur. If the growth is at all vigorous, the renal pelvis is rapidly filled and the ureter is involved either by direct extension or by implants carried in the urinary stream.

As in many other lesions of the upper urinary tract, hematuria is the one characteristic symptom, and its appearance calls for every possible diagnostic procedure. Plain x-ray films may reveal no abnormality. Even when an opaque medium is used, the outline of the pelvis and calyces may appear normal, though Wade (Australian and New Zealand J. Surg. **5:** 3, 1935) states that in delicate soft roentgenograms careful inspection will show a slight alteration in the density of the shadow within the pelvis, suggesting the presence of a tumor. Excretory urography is seldom as satisfactory in these cases as the retrograde method.

Surgical extirpation of the involved kidney with the ureter is the treatment of choice. Preoperative and postoperative irradiation have been advocated but in general the tumors are radioresistant. In the case reported here, Coutard's fractional dose method was attempted, but the patient was unable to endure the treatment and the author's impression was that it would have been of little effect. A nephrectomy was done, followed six weeks later by ureterectomy, and the prognosis was regarded as favorable, since malignant invasion of the ureter could not be demonstrated.

A color plate and other illustrations are included.

Control and Arrest of Lesions of Renal Tuberculosis. Gilbert J. Thomas, Theo. L. Stebbins, and Samuel T. Sandell. J. Urol. **46:** 579–589, October 1941.

Early lesions of renal tuberculosis become quiescent and a few apparently heal. Renal lesions are only a local manifestation of a constitutional disease. Nephrectomy removes only the renal focus. Surgical treatment in no way builds up the patient's resistance to the disease.

The authors do not recommend hygienic treatment as a routine procedure for all lesions of renal tuberculosis. It should be tried, however, when patients have not manifested their ability to control other tuberculous lesions, in those who have other active lesions that may become life-taking, in patients with small renal lesions that do not progress, when the clinical data suggest bilateral renal involvement, and when any doubt exists concerning the correctness of the diagnosis. Intensive bed rest, heliotherapy, and hygienic management control many bilateral lesions so that the patients enjoy years of comfort and useful life. Many of such patients against advice submit to surgery and die within a short postoperative period.

Four cases are presented in which bacilli of tuberculosis were demonstrated in the urine at the time of original diagnosis. Subsequently, during several consecutive examinations, bacilli were not isolated from the urine and none of the findings usually associated with urogenital tuberculosis was observed. In these cases, followed five, eleven, thirteen, and thirteen years, respectively, clinical evidence indicated that the tuberculous process in the kidneys healed or became arrested under an intensive hygienic régime.

The authors conclude by stating that in their opinion the kidneys react toward the destructive effect of the bacillus of tuberculosis as do other organs and tissues, and by asking, if other organs and tissues can control lesions and stop the destructive effect of the bacillus of tuberculosis, why is this impossible for the kidney?

BENJAMIN H. ORNDOFF, M.D.

OBSTETRICS AND GYNECOLOGY

Radiographs and Disproportion. J. V. O'Sullivan and F. M. Crawshaw. Brit. M. J. **2:** 543–544, Oct. 18, 1941.

The authors describe a simple method of estimating maternal pelvic disproportion and of obtaining a prognosis of delivery in obstetrical cases, based on measurements from anteroposterior and lateral films. In all cases analyzed in a large series of disproportions the internal conjugate varied from $3^1/_2$ to $4^1/_2$ inches. Examinations were made weekly toward the end of pregnancy.

The observation is made that where the fetus maintained its original position spontaneous delivery occurred regardless of disproportion. In interpretation of films the lateral view seemed more reliable since the anteroposterior diameter of the brim is best demonstrated and also the fetus suffers the same degree of exaggeration in the film as does the maternal skeleton. In interpreting films, a line is drawn between the promontory of the sacrum and the upper posterior margin of the symphysis; from each end of this line are drawn perpendicular lines, anteriorly, making what is termed a box. In 102 cases, with 6 exceptions, normal delivery occurred where the fetus fitted into the box, but where it did not, artificial delivery was essential. In an addendum by the radiologist, the routine technic in making films is described. This corresponds to the generally accepted rules in such cases

Q. B. CORAY, M.D.

THE SPINAL CORD

Pilonidal Sinuses Occurring over the Higher Spinal Segments with Report of a Case Involving the Spinal Cord. Henry P. Kooistra. Surgery **11:** 63–74, January 1942.

The author analyzes a group of 14 cases of pilonidal sinus involving spinal segments above the sacrococcygeal region, 13 from the literature, and 1 of his own. With a single exception the cases were confirmed by operation. In 12 the lesion extended down to or within the meninges. In the remaining case (the author's) the lesion was intramedullary.

The distribution of the sinuses was as follows: cervical 1, thoracic 5, lumbar 3, sacral 5. In all but 2 patients there was an associated spina bifida. Sex distribution was equal. Ages ranged from three and a half months to twenty years, but only 5 patients were over five years of age.

The signs and symptoms produced by these lesions were primarily neurogenic. As a rule, sinuses occurring over the lower half of the spine became infected and produced either a subdural abscess or a meningitis. These cases manifested all the signs of meningeal irritation. Sinuses occurring over the upper half of the spine usually showed no evidence of infection and presented signs and symptoms typical of a cord tumor. The commonest complaint was difficulty in walking due to spastic paralysis of the lower extremities. Sensory disturbances were usually mild. All the patients showed lack of fusion or rachischisis of the neural arch.

JOHN E. WHITELEATHER, M.D.

Myeloscopy: Intraspinal Endoscopy. J. Laurence Pool. Surgery **11:** 169–182, February 1942.

Four years ago the principle of intraspinal endoscopy was adapted to the diagnosis of lesions affecting the cauda equina and lowermost spinal cord. Since that time, nearly 400 "myeloscopic" examinations have been carried out. The instrument devised for the purpose, a myeloscope, may be introduced between any of the lumbar spinous processes in much the same manner as an ordinary lumbar puncture needle. No known trauma to nerve roots has ensued.

The abnormal conditions recognizable by myeloscopy include varicose vessels, arachnoid adhesions of post traumatic or post-inflammatory origin, neoplasms, the presence of inflamed nerve roots associated with clinical neuritis, and the effects of a herniated nucleus pulposus or hypertrophied ligamentum flavum.

The author describes the myeloscope, which consists of an obturator with light-carrying cannula and a lens system. Fluid can be withdrawn through this instrument. The technic of myeloscopy is outlined, and the appearance of normal structures as seen through the myeloscope is described. Some excellent illustrations in color are reproduced.

The importance of recognizing varicose vessels of the cauda equina lies in the fact that such vascular abnormalities represent a similar condition affecting the spinal cord, for the blood supply of the cauda equina is continuous with that of the spinal cord. Varices may extend the entire length of the cord or may be confined to a few segments thereof. Myeloscopy is therefore indicated in patients having signs of diffuse cord disease of obscure etiology, especially since x-ray treatment is often beneficial in cases of varices.

The congenital type of varicosity generally manifests itself during the first two decades and is distinguished by the fact that the abnormal vessels appear *separate from the nerves*. The acquired varix, which occurs in older persons, is represented by dilatation and tortuosity of the vessels *on the nerves*. These older patients usually give a history of repeated trauma. Possible explanations of post-traumatic varices, which may act alone or in combination to produce the vascular pathology, are gliosis of the cord, constrictive arachnoiditis around the cord, traumatic insult to the vessels themselves.

There are no severe after-effects of myeloscopy. Its value lies in the differential diagnosis between operable and inoperable lesions of the cauda equina and lower spinal cord, in the ruling out of post-traumatic malingering, and in the fact that with its use patients may be spared lipiodol injection or even an exploratory laminectomy.

JOHN E. WHITELEATHER, M.D.

RADIOTHERAPY

MALIGNANT TUMORS

Radioactive Phosphorus as a Therapeutic Agent in Malignant Neoplastic Disease. J. M. Kenney. Cancer Research **2:** 130–145, February 1942.

Preliminary results of the treatment of malignant disease with radioactive phosphorus (P^{32}) are outlined. The amount of the isotope administered depended upon the weight of the persons treated and the condition of their erythropoietic tissue, each course varying from 20 to 100 μc. per kg. A course was divided into 5 to 7 doses. The radioactive material was distributed throughout the body, its effectiveness depending upon differential absorption by tumor cells or differences in radiosensitivity of normal and neoplastic cells. Subtherapeutic tracer doses disclosed differences among tumors, greater absorption occurring in osteogenic sarcoma or lymphosarcoma than in mammary carcinoma. The isotope proved efficacious in the treatment of chronic myeloid or lymphatic leukemia, as it reduced the number of white cells, the size of the spleen and lymph nodes, and the percentage of immature cells in the bone marrow. Of 14 patients in this group 8 survived after eighteen months. Acute leukemia appeared unaffected. Preliminary evaluation of the results in 12 patients with lymphosarcoma revealed regression of the masses in 5. The effects in 8 patients with osteogenic sarcoma, treated by other established methods but given P^{32} with the hope of averting metastases, could not as yet be judged. MILTON J. EISEN, M.D.

Practical Ideas on Treatment of Cancer of the Breast. R. Sarasin. Schweiz. med. Wchnschr. **72:** 97–100, Jan. 24, 1942.

Breast cancers are classified into four stages: (1) local tumor without adenopathy or infiltration of the skin; (2) tumor adherent to the skin and axillary adenopathy; (3) involvement of the chest wall and infiltration of the axillary chain; (4) tumor adherent to the skin and deep fascial planes with fixation and with axillary and supraclavicular node involvement. Stage 3 represents the limit of operability. This grouping differs somewhat from Steinthal's classification in that it puts more emphasis on attachment to the deep structures. Since the discussion has to do with cures, cases with distant metastases to bone or viscera are eliminated.

The author is of the opinion that dissemination of the tumor by irradiation may actually occur, being favored by the therapeutic shock, which may break down local resistance, particularly if the tumor is just at the point of metastasizing, and by the cumulative effect of the radiation procedure added to the previous insult of operation. In accordance with Baclesse, the

two following principles are advocated. (1) Irradiate widely any macroscopic lesion. (2) Treat with a dose as heavy as if destruction of the neoplasm depended on x-ray alone.

The necessity of preliminary consultation between surgeon and radiologist and a co-ordination of their plans is strongly emphasized. For first-stage lesions electrosurgical excision (Halsted operation) is advised. If the lymph nodes are histologically free of cancer, no radiation need be given locally, but in young women roentgen castration is advocated. In cancers in the second stage, operation preceded by irradiation of a wide field including the internal mammary chain of lymphatics, the axilla, and the supraclavicular region, is advised. This treatment should be spread out over several weeks, and the operation done three to five months after the conclusion of irradiation, when the skin reaction is healed. Postoperative irradiation is indicated if microscopic evidence of cancer is found in the excised nodes. In the third stage the same procedure should be followed as in the second, with a high degree of individualization of dosage. Results are better than if postoperative irradiation is employed exclusively. In the fourth stage radiation alone is indicated. If the patient is in good general condition, a full course of treatment should be given. If this causes complete node regression, a radical operation should then be done.

The author condemns as fallacious the belief that time spent in preoperative irradiation and clearing up of the subsequent reaction is wasted and only delays the operation, sometimes until after metastatic spread. He believes the danger of metastasis from cutting through active cancer is the greater of the two. Postirradiation adhesions do not complicate the picture in this disease. LEWIS G. JACOBS, M.D.

Cancer of the Breast: Results of Surgical Treatment at Collis P. Huntington Memorial Hospital. C. C. Simmons. New England J. Med. **226:** 173–178, Jan. 29, 1942.

This is a review of 135 cases of cancer of the breast treated surgically at the Collis P. Huntington Memorial Hospital up to 1936. The criterion of operability was limitation of the lesion to the breast or the breast and axilla. Two cases of cancer of the male breast were encountered in this series. Three patients died postoperatively, a mortality of 1.9 per cent. In a small group treatment is described as "palliative"; in a second group simple amputation of the breast ("incomplete operation") was done where the tumor seemed to be confined to the breast in an elderly patient.

There remain 116 cases in which radical operation was done, with a cure of 5 to 19 years in 50 cases (42 per cent). Where the axilla was not involved (42 cases) there were 31 cures (74 per cent), and where the axilla was involved (in 74 cases) there were 19 cures (25 per cent). On a 5-year basis the cures by surgery alone in the entire group are 55 per cent and in cases without axillary involvement 85 per cent, but the latter group includes cases in which the growth was known to be limited to the breast and simple amputation alone was done. In no patient with uninvolved axillary nodes did recurrence develop after five years.

The median duration in cases with the growth limited to the breast was two months and in those with axillary involvement nine months. The extension of the disease to the axilla is a most vital factor in prognosis. In 59 cases no lymphadenopathy was felt, but cancer was found to be present in 25 of these, an error of 40 per cent. Eighty per cent of palpable nodes proved to be metastatic.

The largest number of cures occurred in cases of low malignancy but there was a greater percentage of cures in tumors of high than in those of medium malignancy. Age had but little influence on the end-result.

Biopsy was resorted to in 25 per cent of the patients and of these 50 per cent are well. In 26 per cent of this group disease was later found to be limited to the breast, but this shows the difficulty of making a correct diagnosis even in extensive disease.

In 9.5 per cent of the entire group there were local recurrences. The commonest remote sites were in bones and lungs (23 per cent each). In 14 cases recurrence took place after five years. In 4 cases the disease had been limited to the breast and recurrence was remote. There is no demonstrable relation between the extent of the disease, the degree of malignancy, or the age of the patient, and the development of late recurrences.

Irradiation of breast cancer is used only in recurrences. In this series postoperative irradiation was applied to two cases without axillary involvement and both are well. Eleven patients with axillary involvement were irradiated and 3 are well. The percentages approximate those for the entire group.

JOHN MCANENY, M.D.

Dosage Control of Interstitial Radium Treatments by Direct Measurement of Skin Dosage Rate. Part I. Treatment of Primary Growth in Carcinoma Mammae. Part II. Treatment of Secondary Carcinoma in Lymph-Nodes of Neck. W. G. Evans and H. D. Griffith. Brit. J. Radiol. **14:** 345–357; 377–385, November and December 1941.

The lack of accurate methods of measurement of interstitial gamma-ray dosage has prevented this method of treatment from being tried to the fullest extent. Since 1935 a method of measuring the dosage on the skin by means of a Sievert type condenser chamber has been used. This has allowed a more accurate standardization of dosage with gratifying results in tumor disappearance and healing.

The general principles observed in planning the treatment for breast carcinoma are: avoidance of trauma to the tumor, irradiation of the entire breast, construction of the dosage-rate contours to suit the shape of the breast, and irradiation to the limit of skin tolerance. To accomplish this a shield is made to fit the shape of the breast. In this shield holes are made to take the implants and also the ionization chamber. This immobilizes the breast during the entire treatment.

Irradiation is carried out until the limits of tolerance of the skin are reached. With radon a total dose of 650 Sievert hours (5,400 r) can be given, using initial dosage rates of 4 to 5 Sievert units (0.5–0.6 r/m.). This is followed by a moist desquamation of a moderate degree of severity.

Direct measurements have been made on models which show that the assumptions of depth dosage and surface dosage relations are substantially correct. The methods of calculating depth dosages are given. The use of the chamber *in vivo* during the treatment enables adjustments to be made for small errors in dosage distribution that may be revealed.

Details of the tumor size, dosage, and results in ten cases are given.

The second installment of this paper deals with the radium treatment of secondary carcinoma of the lymph nodes of the neck. Such treatment the authors do not undertake until the primary lesion has been treated and its site healed to such an extent that it is no longer a focus for gross septic infection of the lymph nodes. The treatment is planned to give complete irradiation of the entire lymph node system on the affected side of the neck, the distribution of radium covering the submental, submaxillary, superior, and inferior deep cervical nodes as a minimum.

The neck is divided into five fields, the radium is distributed to produce approximately uniform dosage-rate readings on the surface of each field, and each field

is irradiated until the limit of skin tolerance is approached. In planning the distribution of the radium one must take into consideration the surface contour of the field, the radium-skin distance, the radium pattern, and the plane of the radium.

The surface of each of the five fields being approximately flat, it is necessary, if the dosage-rate measurements are to be uniform, for the plane of the radium implants to be "flat" to (parallel with) the surface. In tumor-containing fields the implants are placed immediately deep to the tumor and consequently the plane of the radium is at a greater depth than in fields in which no tumor is present. In such fields the needles cannot be inserted correctly by puncture from the surface but a suitably placed incision is necessary. A graph for calculating the amount of radium necessary to produce a dosage rate of 2–3 Imc. on the surface of the field is reproduced.

About five days after the insertion of the radium needles the dosage-rate on the skin of each field is measured with Sievert chambers. As soon as the epidermicidal dose is attained, the radium is removed. The value of the epidermicidal dose at the dosage rates usually obtained is of the order of 600 Imc. hours, so that a treatment commonly extends over periods of the order of 150 to 300 hours, the actual time depending on the value of the dosage-rate figures in each field. Results in a series of patients are given.

SIDNEY J. HAWLEY, M.D.

Ureteral Obstruction Following Irradiation Treatment of Cancer of the Cervix. Paul E. Hoffman. West. J. Surg. **50:** 69–72, February 1942.

The author carefully studied a group of 97 proved cases of carcinoma of the cervix at Stanford University Clinic. All were examined by intravenous pyelography and those showing any ureteral or renal abnormality were further studied by cystoscopy and retrograde pyelography. The following analysis is given.

Clinical Stage of Cancer	Total Cases	Cases with Ureterorenal Pathology
I	13	1
II	23	2
III	40	16
IV	21	13

Retrograde dilatation was unsuccessful in all cases except one. As the stricture in the latter case was 16 cm. above the ureteral orifice, it is supposed this was a benign stricture. The ureteral obstruction is almost always due to neoplastic extension.

SIMON POLLACK, M.D.

Ewing's Tumor: Report of Case Demonstrating Characteristic Periodic Course. C. P. Roberts. New England J. Med. **226:** 90–97, Jan. 15, 1942.

This is a complete and extensive report of a Ewing's tumor of the pelvis in a young medical student who was co-operative and intelligent enough to give adequate response to inquiries. Details are too numerous and important for abridgment and should be studied in full.

The salient clinical features are insidious onset, regular alternation of episodes of pain and periods of comfort, and progressive intensification. The last is a feature of component episodes, as well as of the total course. The history of the tumor is valuable in avoiding the erroneous diagnosis of osteomyelitis. The striking feature of this case is that at the times of reactivation, when new lesions were appearing, old sites of metastasis again became painful.

JOHN MCANENY, M.D.

Mule-Spinner's Cancer. E. M. Brockbank. Brit. M. J. **1:** 622–624, April 26, 1941.

The author discusses the probable etiology of mule-spinner's cancer based on a study of 150 cases in various stages. The incidence of the disease leaves no doubt as to its relation to the occupation and therefore, as the author says, leaves practically no excuse for failure to decrease its occurrence. The mule-spinner works with bare feet in a warm atmosphere which is well saturated with mineral oil. He frequently wears no underclothing and experiences persistent friction on his thighs from oil-saturated overalls. Because of the excess perspiration the natural protective mechanism of the skin is depleted.

The subjects discussed under etiology are: oil on the clothes, oil in the atmosphere, heat and perspiration, friction from clothing, frequent ichthyosis as a contributory factor, want of body cleanliness, and failure to use certain ointments such as lanolin and olive oil as protective measures. Periodical examinations, more careful selection of machine oils, skin protection by proper underclothing, education, and the use of protective ointments are discussed.

Q. B. CORAY, M.D.

NON-MALIGNANT CONDITIONS

Chemotherapy and Roentgen Radiation in Clostridium welchii Infections: Clinical and Experimental Studies. R. L. Sewell, A. H. Dowdy, and J. G. Vincent. Surg., Gynec. & Obst. **74:** 361–367, Feb. 16, 1942.

The authors report investigations, both clinical and experimental, concerning *C. welchii* infections. They suggest the use of an additional term, "gas cellulitis" or "Clostridium cellulitis," to include the mild and borderline cases of such infection. In their study four criteria of selection were used: (1) positive cultures of *C. welchii;* (2) spreading infection; (3) gas in the tissues; (4) discoloration and edema of the involved structures.

In the light of their own experience the authors attempt to evaluate various therapeutic agents. They state that antiserum in the doses they used has only a feeble prophylactic value but gives "acceptable results when used in conjunction with conservative surgery." Antiserum may control the exotoxins from the infection, but the authors believe these are of relative unimportance in comparison with the primary infection.

Surgery was used conservatively. Poor vascular supply to the part involved is the best indication for amputation. Severely traumatized patients are treated conservatively as long as there is no great arterial damage.

The authors are convinced that roentgen irradiation has a definite beneficial effect in the disease and it was used in nearly all of their cases. While their results have not been as good as some that have been published, notably those of Kelly and Dowell (Radiology **37:** 421, 1941), they have been less disappointing than others.

Chemotherapy in the authors' series consisted in administration of sulfonamides, sulfanilamide being used in the earlier cases. Where the patient was treated by this drug alone for a reasonable period before irradiation therapy, the infection was not controlled. In the later group of cases sulfadiazine was used internally and was also applied locally to the wound.

From their study of therapeutic measures against experimentally produced infections in dogs the authors report some rather interesting findings. They find that on an experimental basis at least, roentgen irradiation did not work satisfactorily as a prophylactic measure. A higher percentage of survivals of inoculated animals was obtained when either sulfadiazine or roentgen irradiation was used alone than when the methods were used together, suggesting that there may be an apparent antagonistic effect between the two agents.

On the basis of their clinical and experimental work, the authors conclude that the treatment of choice in

Clostridium welchii infections in normally vascularized parts is conservative surgery coupled with roentgen irradiation or a sulfonamide (sulfadiazine).

[In the experimentally produced infections the difference in percentage of survivals between those treated with roentgen irradiation and sulfadiazine is quite small. Those interested in the exact figures should consult the original article. I. J. M]

IVAN J. MILLER, M.D.

Diagnosis and Treatment of Trigeminal Neuralgia. W. Ryffel. Schweiz. med. Wchnschr. **72**: 61–64, 85–86, Jan. 17 and 24, 1942.

This is a rather full clinical discussion of trigeminal neuralgia with special reference to the various surgical attacks. The only point of major radiological interest is the statement that deep roentgen therapy was successfully used by Dyes (München. med. Wchnschr. **81:** 1603, 1934) in 17 cases of 20; and by Rüsken (Therap. d. Gegenw. **80:** 296, 1939) in 100 cases of 225. The author used radiation in only a few of his early cases; the technic is not given, and the treatment was unsuccessful. LEWIS G. JACOBS, M.D.

Hemangioma of Vertebra Associated with Compression of the Cord: Response to Radiation Therapy. L. Ferber and I. Lampe. Arch. Neurol. & Psychiat. **47:** 19–29, January 1942.

Ferber and Lampe review the literature on hemangioma of the vertebra, and also report their own case, in a 52-year-old white man whose lesion involved the seventh thoracic vertebra. The roentgenograms of the thoracic portion of the spine revealed the typical vertical striations of the vertebral body produced by hemangioma. The site of the lesion was further substantiated by lipiodol studies.

Of the 52 cases of vertebral hemangioma associated with compression of the cord which are reported in the literature, 12 were treated with roentgen rays with excellent results. The authors treated their patient through a 13 × 15-cm. portal, giving 200 r daily, measured in air, until a total dose of 2,400 r had been administered. Eight months later a second series of treatments was given, totalling 2,000 r in 200 r daily doses to a 13 × 15-cm. field directed to the seventh thoracic vertebra. Their patient made an excellent recovery.

Radiosensitivity of Adamantinoma. H. T. Kimm. Chinese M. J. **59**: 497–507, June 1941.

The author cites some of the conflicting reports in the medical literature regarding the response of adamantinoma to radiation. Nine cases treated at the Peiping Union Medical College were studied in tissue sections before and after treatment by radon, and roentgen rays, or both. In no instance was there convincing clinical evidence of regression, though in two cases some slight decrease in size of the tumors resulted. Histologic changes were observed, but highly differentiated adamantine elements were not materially affected. The author concludes that fully differentiated adamantinomata are highly radioresistant but that the undifferentiated tumors, such as those of the basal-cell type, appear to be comparatively radiosensitive. Radical excision still remains the best form of treatment.

WM. H. GILLENTINE, M.D.

EXPERIMENTAL STUDIES

Effect of Radioactive Phosphorus on the Viability of Mouse Sarcoma 180. K. Sugiura. Cancer Research **2:** 19–24, January 1942.

The effectiveness on mouse sarcoma 180 of radiations emitted by radioactive phosphorus was investigated by immersing tumor fragments in solutions of increasing concentration of the radioactive element (P^{32}). After these mixtures had been kept at ice-box temperatures for periods up to forty-eight hours, the growth capacity of the neoplastic cells was determined by inoculation into animals. Some inhibition occurred after exposure to solutions containing 75 μc. per c.c. The viability of the tumor was completely destroyed by a concentration of 150 μc. In terms of equivalent roentgens these quantities would equal 3,500–6,500 r. Doses of 2,800–3,000 r roentgen rays at 200 kv. are required to kill sarcoma 180 *in vitro*, but the apparent discrepancy in the potency of the two sources of radiation energy may depend upon the known absorption by tumor fragments of only one-half the concentration of the radioactive isotope in the surrounding fluid.

MILTON J. EISEN, M.D.

Comparative Studies on the Radiosensitivity of Normal and Malignant Cells in Culture. I. The Effect of X-Rays on Cell Outgrowth in Cultures of Normal Rat Fibroblasts and Rat Benzypyrene-Induced Sarcoma. L. Halberstaedter, G. Goldhaber, L. Doljanski. Cancer Research **2:** 28–31, January 1942.

Exposure of explants of normal fibroblasts of the rat and cells of a sarcoma induced in this animal by benzpyrene revealed identical radiosensitivities. In either case growth was inhibited completely by doses of 200,000 r. MILTON J. EISEN, M.D.

Effect of Thorium Dioxide on Normal and Estrinized Tumor-Bearing Rats. J. Heiman. Cancer Research **2:** 25–27, January 1942.

Colloidal thorium dioxide was injected into rats bearing spontaneous or transplanted mammary fibroadenoma. Some animals received in addition treatment with estrogen, but in no instance was malignant transformation of the benign tumor observed. A few sarcomas were produced by the radioactive substance.

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